The New England
Journal of Medicine

Copyright, 1944, by the Massachusetts Medical Society

Volume 231 NOVEMBER 2, 1944 Number 18

PENICILLIN IN SULFONAMIDE-RESISTANT GONORRHEA*

A Review of 200 Cases

LIEUTENANT COMMANDER N. S. SCARCELLO (MC), U.S.N.R.

ST. ALBANS, LONG ISLAND, NEW YORK

ALTHOUGH penicillin was discovered in 1929 by Fleming,[1] its use in clinical work did not take place until 1940. In that year a group of Oxford investigators[2] published a paper entitled "Penicillin as a Chemotherapeutic Agent." This was followed in 1941 with another report on the practical use of penicillin.[3] From then on, reports of the miraculous effect of the drug have been increasing daily. Limited supplies were insufficient for all investigators, and since penicillin was being manufactured under government supervision, it was reserved chiefly for military use.

It was early recognized that penicillin has a definite place in sulfonamide-resistant cases.[4, 5] This was proved by tests with sulfonamide-resistant organisms and by treating sulfonamide-fast cases of gonorrhea.[6]

Permission to use penicillin at the United States Naval Hospital in St. Albans, Long Island, was given in July, 1943, by the Bureau of Medicine and Surgery. To affect the maximum utilization of the limited quantities available, it was directed that it be used in cases of sulfonamide-resistant gonorrhea. These were cases that had failed to respond to two courses of sulfonamides, each course consisting of at least 20 gm. of the drug.

PHARMACOLOGY

Penicillin is produced from the mold *Penicillium notatum*. It is supplied in sterile ampoules as a sodium salt for clinical use and appears as a yellow or light-brown amorphous powder. It is readily soluble in water and in saline and glucose solutions, and is subject to deterioration if exposed to high temperatures or even to room temperatures for an extended period of time. It is stable to light, but must be kept stored at a temperature below 5°C. — whether in powder form or in solution. It is readily absorbed when given by the intramuscular route and more slowly when given subcutaneously, and is rapidly excreted through the urinary tract,[7] a large part of the injected drug being lost within a few hours. This must be kept in mind to obtain the best results and to maintain a sufficient concentration of the drug within the blood stream. It must be given in sufficient doses and at frequent regular intervals, as may be required for the specific infection under treatment.

Although penicillin has a powerful bacteriostatic action,[8, 9] it has been found to have some bactericidal action as well. It is remarkably effective in the treatment of infections produced by *Staphylococcus aureus*, pneumococci and hemolytic streptococci. In general, penicillin is not effective against gram-negative organisms. Exceptions to this rule are the gonococci and meningococci. The gonococci, especially those in the sulfonamide-resistant group, appear to be remarkably susceptible.

Penicillin has so far proved to be nontoxic.[10–12]

METHOD OF STUDY

This paper is a review of 200 cases of sulfonamide-resistant gonorrhea treated with penicillin, in the majority of which a sulfonamide drug had been given for at least two weeks, representing a total of 40 gm. The periods of sulfonamide therapy were as follows: in 6 cases, at least one week; in 44 cases, two weeks; in 35 cases, three weeks; in 34 cases, four weeks; in 18 cases, five weeks; in 23 cases, six weeks; in 23 cases, seven weeks; in 6 cases, eight weeks; in 4 cases, nine weeks; and in 7 cases, ten weeks.

On entry all the patients had a positive urethral or prostatic smear or culture, or both. One hundred and twenty-nine patients had a marked urethral discharge, 16 a moderate discharge, 46 a slight discharge, and 9 either a "morning tear" or a positive prostatic culture.

Using the two-glass test, the second sample was clear in approximately 75 per cent of the pa-

*From the Urological Department, United States Naval Hospital, St. Albans, Long Island.

Read at a meeting of the New England Section of the American Urological Association, Boston, April 27, 1944.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

tients, which indicated that the infection, although not cured by the sulfonamide therapy, had been confined to the anterior urethra.

On entry, smears were taken in all cases and a two-glass test was done. While waiting for penicillin, and if there were no contraindications, the patients were given either sulfathiazole or sulfadiazine.

The penicillin was dissolved in sterile distilled water, 20 cc. of water to each 100,000 units. All the medication was given intramuscularly, with the buttocks being the site of choice and the injections alternated between them. At present, the patients receive five injections of 4 cc. (20,000 units) each at two-hour or three-hour intervals, with restriction of fluid, for a total of 100,000 units, this so-called "course" having been found to give the best results. Although there was an occasional complaint of soreness, this was no more than was to be expected with intramuscular injections, and was probably due to the giving of repeated injections in the same area. No complications followed this mode of administering the drug.

Clinical Results

As is shown in Table 1, the total dosages of the initial courses varied, owing to the trial of different amounts. There were 27 cases (14 per cent) requiring two or more courses of penicillin. There were no failures, and all the cases cleared up after the second or third course. The criterion followed for a so-called "clinical cure" was two negative prostatic cultures and smears. This regime was carried out so far as possible with due consideration to military exigencies and to the jeopardizing of the patient's condition.

Table 1. *Amounts of Penicillin Administered.*

No. of Cases	Dosage of Initial Course	Cases Requiring Repeat Courses*	
		No.	Percentage
	units		
18	150,000	1	6
15	120,000	0	0
63	100,000	8	13
31	75,000	5	16
15	60,000	4	27
56	50,000	7	13
2	30,000	2	100

*Repeat courses were given to patients who continued to have a discharge or a positive prostatic culture following the first course of penicillin.

More than 80 per cent of the patients had no visible urethral discharge twenty-four hours after the first course, but a few had a mucoid discharge for three or four days.

As shown by Table 1, the percentage of cases requiring repeat courses was less when large initial courses were given. Ninety-six patients received 100,000 or more units in the initial course, and only 9 of them (9 per cent) required repeat courses. There were 104 patients who received 80,000 or less units, 18 of whom (17 per cent) required repeat courses.

The average number of hospital days in this series was reduced to approximately a third of that usually to be expected.

Analysis of Repeat-Course Cases

In the following section, the cases requiring repeat courses are analyzed in brief reports, which are divided according to the number of units of penicillin given in the initial course.

Of the cases requiring repeat courses, 18 cleared up following the first repeat course, 7 required two repeat courses, and 2 needed three repeat courses.

150,000-Unit Group

Case 79. The patient had received sulfonamide therapy for 4 weeks, with no apparent clinical improvement. He did not respond well to the first course of penicillin. Four days after its administration, he developed an acute epididymitis, which was treated symptomatically. Discharge still persisted, so that a second course of 60,000 units was given 4 weeks after the first one, and the patient subsequently improved.

100,000-Unit Group

Case 68. The patient, a Negro, had previously received sulfonamide therapy for 5 weeks. Although the discharge cleared following the first course of penicillin, he continued to have a positive prostatic culture, so that a second course was given 3 weeks after the first, following which cultures became negative.

Case 78. The patient had received sulfonamide therapy for 6 weeks. Following the first course of penicillin (60,000 units), prostatic cultures remained positive, and a repeat course was given 10 days later. Cultures then became negative.

Case 82. The patient, a Negro, had received sulfonamide therapy for 9 weeks. Positive cultures persisted following the first course of penicillin, although clinically he appeared cured, with no discharge and a clear urine. Two weeks after the first course, a second one of 60,000 units was given, followed by a third of 100,000 units 2 weeks later, after which negative cultures were obtained.

Case 87. The patient, a Negro, had received sulfonamide therapy for 9 weeks. After the first course of penicillin the discharge ceased and the urine cleared, but the prostatic smears remained positive, and 10 days later the discharge recurred. A second course of 50,000 units was given, following which the discharge ceased and the cultures became negative.

Case 89. The patient had received sulfonamide therapy for 7 weeks. After the first course of penicillin the discharge, although slight, persisted for 1 week. A second course of 25,000 units was given and the patient became clinically cured.

Case 114. The patient had received sulfonamide therapy for 5 weeks. The discharge, although diminished, persisted after the first course of penicillin, but cleared up immediately following the administration of a second course of 25,000 units.

Case 142. The patient had received sulfonamide therapy for 7 weeks. On entry his condition was complicated by an acute epididymitis. The discharge persisted after the first course of penicillin and the cultures remained positive. A second course (25,000 units) was given, with no improvement 2 weeks later. A third course was given 1 week later, with no clinical improvement. One week later a fourth course of 50,000 units was given, and the smears and cultures became negative.

Case 167. The patient had received sulfonamide therapy for 4 weeks. A slight discharge persisted following the first course, and a second course of 25,000 units was given, with excellent results.

75,000-Unit Group

Case 77. This case was complicated by a prostatic abscess and moderate retention. The patient had received sulfonamide treatment over a period of months, along with irrigations and instillations. The first course of penicillin cleared the acute symptoms and retention almost immediately. The discharge recurred 1 week later, and a second course (60,000 units) was given, with excellent results.

Case 86. The patient had received sulfonamide therapy for 3 weeks. Following the first course of penicillin, the discharge persisted and the cultures and smears remained positive. A second course (25,000 units) was given 2 weeks later, with no apparent improvement. Two weeks later a third course (50,000 units) was given with excellent results.

Case 144. The patient, a Negro, had received sulfonamide therapy for 3 weeks. The discharge persisted following the first course of penicillin, but cleared up immediately when 25,000 units was given 2 weeks later. The patient went A.W.O.L., and on return had a discharge. A third course (25,000 units) brought a good response.

Case 165. The patient had received sulfonamide therapy for 5 weeks. The discharge persisted following the first course of penicillin, but after a second course 6 days later it cleared and the patient improved.

Case 176. The patient had received sulfonamide therapy for 5 weeks. He responded poorly to the first course of penicillin, the discharge continuing and the cultures remaining positive. A second course (25,000 units) produced excellent results.

60,000-Unit Group

Case 69. The patient had received sulfonamide therapy for 3 weeks. The discharge persisted following the first course of penicillin, and two weeks later an acute epididymitis developed. Four weeks after the first course, a second one (70,000 units) was given, with good results.

Case 74. The patient had received sulfonamide therapy for 10 weeks. The discharge persisted following the first course of penicillin. A second course was given 4 days later and had no effect, and a third was given 4 days after the second, with good results.

Case 80. The patient had received sulfonamide therapy for 10 weeks. The first course of penicillin failed to stop the discharge, and the cultures were positive, so that a second course (30,000 units) was given, with good results.

Case 171. The patient, who entered the hospital with a severe acute epididymitis, had received sulfonamide therapy for 2 weeks. He did not respond well to the first course of penicillin, and a second course (30,000 units) was given 8 days later, but the smears remained positive. A third course (25,000 units) was given 2 weeks later. Following this the cultures became negative, but the discharge recurred, and a fourth course (50,000 units) was given, with good results.

50,000-Unit Group

Case 99. The patient, a Negro, had received sulfonamide therapy for 2 weeks. The first course of penicillin resulted in negative cultures and smears, and a second course (50,000 units) 2 weeks later stopped a recurrent discharge.

Case 101. The patient had received sulfonamide therapy for 2 weeks. A second course (40,000 units) was necessary to control the profuse discharge that the first course of penicillin had failed to control.

Case 110. The patient had received sulfonamide therapy for 5 weeks. There was a recurrence of the discharge 1 week after the first course of penicillin, so that a second course (25,000 units) was given, with a good effect.

Case 123. The patient had received sulfonamide therapy for 10 days. Owing to a persistent slight discharge following the first course, a second course (25,000 units) of penicillin was administered and produced a clinical cure.

Case 135. The patient had received sulfonamide therapy for 2 weeks. The first course of penicillin produced good results, except that the patient developed a "morning drop." A second course (50,000 units) was given, with immediate good results.

Case 143. The patient had received sulfonamide therapy for 6 weeks. The cultures remained positive after the first course of penicillin. A second course (30,000 units) resulted in clinical cure.

Case 184. The patient had received sulfonamide therapy for 12 days. The discharge recurred 4 days after the first course of penicillin, and the cultures remained positive. A second course (30,000 units) given 5 days later was followed by good results.

30,000-Unit Group

Case 112. The patient, a Negro, had already been discharged clinically cured after a course of 60,000 units of penicillin. On readmission he was given sulfonamide therapy followed by 30,000 units of penicillin, with poor results. One week later a second course (25,000 units) was given, but positive cultures were obtained only after a third course (30,000 units).

Case 141. The patient, a Negro, had received sulfonamide therapy for 2 weeks. Although cultures became negative after the first course of penicillin, the discharge kept recurring, so that a second course (35,000 units) was given 3 weeks later. A third course (100,000 units) 1 week later produced good results.

Complications

Twenty-nine patients had complications on entry or developed them while in the hospital.

There were 3 patients with gonorrheal arthritis who received penicillin, and all had an immediate good response.

There were 4 cases of prostatic abscess, and all the patients showed an immediate good response to penicillin therapy.

Seventeen patients had an acute epididymitis on entry, and 5 developed epididymitis following penicillin. Penicillin had little or no apparent effect on this condition. All the patients required symptomatic treatment and bed rest, and the course of the epididymitis was not shortened by penicillin.

Discussion

Penicillin has so far lived up to the predictions made for it, and has a definite place in the treatment of cases of sulfonamide-resistant gonorrhea.

No toxic reactions were noted in this series.

The Negro patients did not respond well to the drug, and approximately half of them required a repeat course.

Penicillin had little noticeable effect on the cases complicated by epididymitis, although immediate good results were obtained in the cases with gonorrheal arthritis and prostatic abscess.

The patients receiving initial courses of large dosage (100,000 units) required fewer repeat courses than those who were given smaller dosages and such a dosage should be used whenever possible.

Sulfonamide therapy should be continued as long as possible to keep the infection localized, even though clinical improvement is not noted. Irrigations and instillations, the cause of the majority of complications, should be avoided whenever possible.

The question of chancre should always be kept in mind, since some observers have found that

treatment with penicillin obscures the detection of a chancre in its early stages.

There were 2 patients in this series who, although they had received 60,000 units of penicillin, had been suspected of having a chancre. One case was diagnosed by dark-field examination, but in the other it was necessary to wait for the blood to become serologically positive. In the latter, a dorsal slit showed a scarred area on the corona that was apparently a healed lesion.

There were apparently only 2 patients in this series who had previously had gonorrhea. This is misleading, owing to the fact that once men are returned to duty, they may be hospitalized in any part of the world, making a thorough follow-up impossible.

Summary

Two hundred cases of sulfonamide-resistant gonorrhea treated with penicillin have been reviewed and the findings and results tabulated. There were no toxic reactions, and all the patients were able to return to duty.

Penicillin has definitely proved its worth in the treatment of such cases. It has made it possible to return these patients to duty in one third of the time previously required.

References

1. Fleming, A. On antibacterial action of cultures of penicillium, with special reference to their use in isolation of *B. influenzae*. *Brit. J. Exper. Path.* **10**:226-236, 1929.
2. Chain, E., Florey, H. W., Gardner, A. D., Heatley, N. G., Jennings, M. A., Orr-Ewing, J., and Sanders, A. G. Penicillin as chemotherapeutic agent. *Lancet* **2**:226-228, 1940.
3. Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., Jennings, M. A., and Florey, H. W. Further observations on penicillin. *Lancet* **2**:177-188, 1941.
4. Powell, H. M., and Jamieson, W. A. Response of sulfonamide-fast pneumococci to penicillin. *Proc. Soc. Exper. Biol. & Med.* **49**:387-389, 1942.
5. Tillett, W. S., Cambier, M. J., and Harris, W. H., Jr. Sulfonamide-fast pneumococci. Clinical report of two cases of pneumonia together with experimental studies on effectiveness of penicillin and tyrothricin against sulfonamide-resistant strains. *J. Clin. Investigation* **22**:249-255, 1943.
6. Herrell, W. E., Cook, E. N., and Thompson, L. Use of penicillin in sulfonamide-resistant gonorrheal infections. *J. A. M. A.* **122**:289-292, 1943.
7. Rammelkamp, C. H., and Keefer, C. S. Absorption, excretion and toxicity of penicillin administered by intrathecal injection. *Am. J. M. Sc.* **205**:342-350, 1943.
8. Florey, H. W., and Florey, M. E. General and local administration of penicillin. *Lancet* **1**:387-397, 1943.
9. Herrell, W. E., and Heilman, D. Tissue culture studies on cytotoxicity of bactericidal agents. III. Cytotoxic and antibacterial activity of gramicidin and penicillin; comparison with other germicides. *Am. J. M. Sc.* **206**:221-226, 1943.
10. Keefer, C. S., Blake, F. G., Marshall, E. K., Jr., Lockwood, J. S., and Wood, W. B., Jr. Penicillin in treatment of infections. *J. A. M. A.* **122**:1217-1224, 1943.
11. Florey, H. W., and Jennings, M. A. Some biological properties of highly purified penicillin. *Brit. J. Exper. Path.* **23**:120-123, 1942.
12. Robinson, H. J. Toxicity and efficacy of penicillin. *J. Pharmacol. & Exper. Therap.* **77**:70-79, 1943.

STUDIES IN MEDICAL SOCIOLOGY

III. The Relation of Mental Disorders to Race and Nationality

Major Robert W. Hyde, M.C., A.U.S., and Staff Sergeant Roderick M. Chisholm, A.U.S.

BOSTON

RACIAL and national differences in admission rates to mental hospitals have been frequently studied, but there has never been an extensive study of such differences in the rate of mental disorders found in the population at large. The examination of selectees for induction into the armed forces provides a clear picture of the mental disorders in a cross section of the population, since selectees present the most unselected male group obtainable. The present study, based on data derived from the psychiatric examinations at the Boston Armed Forces Induction Station, shows the variation in rates for the major psychiatric disorders in communities grouped according to predominant nationality. An attempt is made to explain on a cultural basis those disorders that appear clearly to be connected with the predominant races or nationalities studied.

Methods of Study

Selectees from the eastern segment of Massachusetts within thirty-five miles of the coastline were examined at the Boston Armed Forces Induction Station. The period covered was the winter, spring and summer months of 1941 and 1942, wherein 60,000 consecutive selectees were examined. A great diversity of population density is represented, at its greatest in Boston and least in the areas of Cape Cod and the farming areas to the north and south of Boston. Most of the area studied is highly industrialized, with a diversity of mills and factories, but significant sectors are devoted to farming and fishing. The age range of the selectees was from eighteen to forty-four, with most of them between twenty-one and thirty-eight. All social strata were represented, and the group may be said to form a representative cross section of the male population at large.

The people of the area represented a wide variety of nationalities. A few communities were of almost pure English stock, now in the sixth and seventh generation in this country; others, particularly in the dense areas, were of almost completely foreign parentage. The first extensive immigration after colonial times was that of the Irish in the middle of the nineteenth century. Since that time numerous Italians have moved into the commercial areas of Boston and other coastal towns. The Portuguese have moved into the fishing villages of Cape Cod and into Fall

River and New Bedford, and Russian Jews into Boston's commercial and residential districts. The greatest proportion of the Chinese arrived here from China within the last decade. Many of the Negroes came from the South during the depression in the 1930's. The Chinese have settled in one of the densest areas of Boston, and the Negroes in a moderately dense area of that city.

The psychiatric examination, described elsewhere,[1] was necessarily brief. Mental deficiency was determined by a team of psychologists. The most important causes of psychiatric rejection were mental deficiency, psychopathic personality, chronic alcoholism, psychoneurosis and psychoses. It is with these major disorders that this study is concerned.

The number from each community disqualified for each of these mental defects was ascertained. Selectees are grouped in specific communities by Selective Service boards. Each board represents either a city ward in a large city, part of a small city, a large town or several adjacent small towns. Although these artificial community groupings are probably not the best obtainable, they correspond to fairly distinct community entities.

In the consideration of race and nationalities, only those communities were included wherein the majority of the selectees were of the same general nativity. Our findings are doubtless influenced to some extent by the fact that a minority of different mixed nationalities is represented in each community. One advantage of a community consideration, however, is the fact that persons of a given nationality in an immigrant community retain more of the characteristics and habits of that nationality than do those who have scattered as a minority into American communities. The data concerning the Irish, Italian, Portuguese, Jews and Old Americans are derived from a community consideration. Those concerning the Negroes and Chinese are based on a consideration of Negro and Chinese selectees, irrespective of community groupings here, since none of the groupings represented are predominantly Chinese or Negro.

The population density and socioeconomic level of each community were estimated. In preceding studies[2,3] the extent to which these factors are relevant to the incidence of mental disorders has been outlined. It was therefore possible to isolate the psychiatric differences that may have been due to racial or national factors from those that were apparently due to economic status or to population density.

Results

Table 1 shows the variation of comparative rejection rates for the major mental disorders found in selectees from the communities of different predominant nationalities. The average density and socioeconomic level of each group of communities of similar nationality are also noted so that corrections can be made for differences that may be traceable to these causes. Socioeconomic ratings vary from A (best) to F (poorest). The most outstanding figures are the exceptionally high rate of disorders among the Negroes and Chinese. This is especially noteworthy in view of the fact that the figures for these two groups are based on individuals and therefore are not distorted by minorities of other nationalities. The table also shows that there is an obvious parallelism between the total mental disorders and the population density and socioeconomic level of each community represented. This parallelism is so marked that the table cannot be considered to present a clear picture of racial or national differences as such. The significance of racial and national differences becomes evident only when one considers the distribution of different mental disorders within each national grouping.

Table 1. *Relation of Percentage Rejected for All Major Psychiatric Causes to the Predominant Nationality of the Community.*

Nationality	No. Examined	Rejection Rate %	Population Density	Socioeconomic Level
Negro	1212*	37.2	High	F–
Chinese	322*	31.6	High	F–
Italian	3472	13.7	Varied	E
Irish	2440	12.8	High	F
Portuguese	2085	10.4	Medium	E
Jewish	1869	9.4	Medium	D
Old American	1640	5.7	Low	B

*Not community but individual figures.

The Irish communities show high rates of psychopathic personality and chronic alcoholism (Table 2). These communities are high in density — from 10,000 to 20,000 per square mile — and are of the lowest (E and F) desirability. This fact may account for their high rate of psychopathy. The rate for chronic alcoholism cannot be similarly explained, since the Chinese, who live in a community that is at least as dense and as undesirable economically as those of the Irish, show an absence of alcoholism. Studies of hospital admissions have confirmed the findings that the rate of alcoholism

among the Irish is probably higher than those among other national groups for whom statistics are available.[4] During World War I, the Irish showed a significantly high rejection rate for so-called "alcoholic psychoses."[5]

TABLE 2. *Mental Disorders in Irish Communities.*

DIAGNOSIS	REJECTION RATE %
Psychopathic personality	5.9
Chronic alcoholism	3.0
Psychoneurosis	2.5
Mental deficiency	1.2
Psychoses	0.3

Four Italian communities are represented. One of them is low in density, having from 1000 to 2000 persons per square mile, 1 is intermediate, and 2 are high, being over 20,000. The two densest communities are also of the lowest socioeconomic level (F). The least dense of the 4 communities has a desirability rating between D and E, and the other community has a C rating. The most noteworthy features of the Italian pattern are the high rate of mental deficiency and, as compared with the Irish, the relatively low rate of chronic alcoholism (Table 3). There is also a significant difference between the Italians and the Irish in the incidence of psychopathy and psychoneurosis.

TABLE 3. *Mental Disorders in Italian Communities.*

DIAGNOSIS	REJECTION RATE %
Psychopathic personality	4.5
Mental deficiency	3.9
Psychoneurosis	3.8
Chronic alcoholism	1.2
Psychoses	0.4

Four Portuguese communities are represented. Two are low in density (from 2000 to 5000), 1 is intermediate (from 5000 to 10,000), and 1 is moderately high (from 10,000 to 20,000). They range in desirability from C to E, inclusive. In contrast to the Italian pattern, psychoneurosis is the primary cause of psychiatric rejection and psychopathy is less important (Table 4). The Portuguese rate of mental deficiency is comparable to that of the Italians. The incidence of mental deficiency among the Portuguese and Italians cannot be explained wholly in terms of economic level or population density.

TABLE 4. *Mental Disorders in Portuguese Communities.*

DIAGNOSIS	REJECTION RATE %
Psychoneurosis	4.1
Mental deficiency	3.1
Psychopathic personality	2.4
Chronic alcoholism	0.6
Psychoses	0.1

There are three Jewish communities, 1 in the highest density (over 20,000) and 2 intermediate (from 10,000 to 20,000); 1 is at desirability level D, 1 between D and E and 1 at E. The most interesting findings are the high rate of psychoneurosis and the low rate of alcoholism (Table 5). In United States draft statistics for the last war, the Jews were highest in psychoneurosis and among the lowest in "alcoholic psychosis,"[5] and peacetime hospital statistics confirm these findings.[6] Population density and socioeconomic level do not provide a satisfactory explanation of this pattern of mental disorders.

TABLE 5. *Mental Disorders in Jewish Communities.*

DIAGNOSIS	REJECTION RATE %
Psychoneurosis	5.2
Psychopathic personality	2.6
Mental deficiency	1.0
Psychoses	0.4
Chronic alcoholism	0.2

Boston's Chinatown is at the lowest desirability level and has a population density of over 20,000 per square mile. Although some of the Chinese registrants live elsewhere, the majority considered do live in Chinatown. The most interesting findings in Table 6 are the disproportionately high rate of mental deficiency, the low rate of psychopathy and the absence of alcoholism. This pattern, which cannot be explained on the basis of community desirability or population density, provides striking evidence of the significance of racial or national factors.

TABLE 6. *Mental Disorders Among Chinese.*

DIAGNOSIS	REJECTION RATE %
Mental deficiency	24.5
Psychoneurosis	5.9
Psychopathic personality	1.2
Chronic alcoholism	0.0
Psychoses	0.0

The term "mental deficiency" as applied to the Chinese is somewhat unfortunate, since the majority of the Chinese who are called mentally deficient are probably not feeble-minded in the ordinary usage of the term, but, as will be explained, are under so severe a cultural handicap that they are judged unable to absorb military training.

No single community represented among Selective Service boards is predominantly Negro. Although most of the Negroes live in dense communities of the lowest socioeconomic level, it is impossible to make proper corrections for socioeconomic

level and population density. It is not known whether the Negroes are forced to live at a level below that of the other population of the same community. The exceptionally high rate of mental disorders among them cannot be explained merely on the basis of population density or socioeconomic level. The Negroes show the highest rate for psychopathy and psychoneurosis and, next to the Chinese, the highest rate for mental deficiency (Table 7).

TABLE 7. *Mental Disorders Among Negroes.*

DIAGNOSIS	REJECTION RATE
	%
Psychopathic personality	16.3
Mental deficiency	11.7
Psychoneurosis	6.7
Chronic alcoholism	2.2
Psychoses	0.3

The Old Americans are subject to fewer stresses than are any of the other groups here considered. Their pattern of disorders (Table 8) appears to be adequately explained on the basis of the high socioeconomic level and intermediate population density of their communities.

TABLE 8. *Mental Disorders in Old American Communities.*

DIAGNOSIS	REJECTION RATE
	%
Psychoneurosis	2.7
Psychopathic personality	1.5
Mental deficiency	0.7
Chronic alcoholism	0.4
Psychoses	0.4

DISCUSSION

Tables 1 through 8 indicate in general that, although density and economic level may be of major importance in the etiology of mental disorders, there are significant variations that can be explained only by reference to factors related to race or nationality. We shall attempt to show which differences are directly related to differences in density and economic level and which require reference to racial or national factors. In suggesting a cultural explanation of these variations, no attempt is made to minimize the importance of biology and heredity. Heredity and environment are so entwined that it is extremely difficult to weigh their relative importance. A community study of this sort, however, presents an excellent opportunity to note the significance of environmental factors. So little is known at the present time about the etiology of mental disorders that the best one can attempt to do is to suggest the lines that an adequate explanation ought to take.

It is assumed that the so-called "functional" mental disorders are manifestations of the emotional stress and tension that result when the individual has been subjected to abnormal deprivations and frustrations. The most primitive outlets to stress are those of aggressiveness, belligerency, acquisitiveness, sexual freedom and other asocial conduct falling under the term "psychopathic personality." Chronic alcoholism is another primitive outlet, which may either be associated with aggressiveness or act as a substitute for it. When this type of outlet is blocked, the stress may manifest itself in another form. With cultural taboos against asocial conduct or alcoholism, stress may turn itself inward and the subject may then become psychoneurotic. Mental disorders thus depend partly on the acceptability of the outlet for stress.

Mental disorders also seem to depend upon the type of stress to which the individual is subjected. Aggressiveness follows on the frustration of elementary physical needs, but usually not frustration of more developed or "intellectual" needs. In the lowest economic level, where these higher-type needs have not had the opportunity to develop, the natural and accepted outlet to stress is psychopathy. In the more desirable communities where it is mainly the higher-type desires that are frustrated, the natural outlet is psychoneurosis. Indeed, as a rule it is only in the communities at the lowest point on the desirability scale, the F communities, that psychopathy prevails; one need only move up one step, to the E communities, to note a marked change in the pattern of mental disorders.

In addition to the frustrations and deprivations that are related directly to high population density and low socioeconomic level, there are further sources of stress to which most of the racial groups here considered are subject. When people are transplanted into a new and unfriendly environment, requiring different cultural standards and patterns of conduct, they are subject to varying difficulties of adaptation. Social and racial prejudice leads to inequality in the opportunities for jobs and housing, and suspicion and insults suffered at the hands of the dominant native population breed feelings of inferiority and resentment. When the prejudice is intense enough, the immigrants withdraw into segregated and isolated groups. Parents attempt to bring up their children according to the precepts of their Old World culture, at the same time that the children are attending American schools, speaking English and becoming Americans in appearance, habits and customs. The children are expected to adjust themselves to divergent cultures, and the resultant conflict tends to create both humiliation and disrespect for authority.

Numerous studies have shown that crime and delinquency rates are higher among the second generation than among the immigrant parents.[7–9] Levy[10] has attributed this to the conflict between

the demands of the parents and the demands of society. Klineberg[11] remarks that the very fact that criminality "appears in the second and not in the first generation makes it clear that it cannot have a racial or biological basis, since this is obviously the same for both groups."

Large numbers of Italians, Negroes, Portuguese and Chinese have migrated from rural to urban communities. In rural communities there is little organized control of the individual's conduct other than that enforced by the social pressure of the group. The influence of law is unimportant, weak or resented. There is more respect for common labor, fewer broad class barriers based on material wealth, greater physical security and less concern for luxuries. These values are changed with movement into urban society. Because of the extent of adaptation necessary in the changing to a greatly divergent cultural pattern, this rural-urban shift usually brings cultural disorganization, with attendant increase in crime, delinquency, alcoholism, ambition and selfishness.

These stresses provide a plausible explanation of some of our findings. This is evident in racial and national variations in psychopathy and psychoneurosis, in the marked differences in the incidence of chronic alcoholism and in the disproportionately high rate of mental deficiency in some national groups. Sufficient data on the psychoses to warrant any generalization are not available.

The high incidence of psychopathy among the Negroes, Irish and Italians (Table 9) is easily explained. Each of these groups is subject to the stresses that accompany population density and low socioeconomic level. They are immigrant groups and, in varying degrees, have met with suspicion and hostility on the part of the Old Americans. Large numbers of them have undergone the disorganization involved in a rural-urban shift. The Italians, and particularly their children, — the generation now being examined for induction, — have been submitted to a conflict between American society and the culture of their parents. The Negroes have been severely oppressed by all the frustrations and deprivations mentioned above, as well as by many others. Psychopathy is the natural reaction to such stress, and it is acceptable in the undesirable communities from which most of these people come.

TABLE 9. *Differences in Rejection Rates for Psychopathic Personality and Psychoneurosis in Communities of Different Predominant Nationalities.*

PSYCHOPATHIC PERSONALITY		PSYCHONEUROSIS	
NATIONALITY	REJECTION RATE %	NATIONALITY	REJECTION RATE %
Negro	16.3*	Negro	6.7*
Irish	5.9	Chinese	5.9*
Italian	4.5	Jewish	5.2
Jewish	2.6	Portuguese	4.1
Portuguese	2.4	Italian	3.8
Old American	1.5	Old American	2.7
Chinese	1.2*	Irish	2.5

*Not community but individual figures.

Since the Irish and the Italians have a culturally acceptable outlet in psychopathy, the rate for psychoneurosis is correspondingly low. It is lowest among the Irish, possibly because they find a further outlet in alcoholism. Psychoneurosis is the primary cause of psychiatric rejection among the Portuguese, whereas psychopathy is the primary cause among the Irish and Italians. This probably can be explained in terms of socioeconomic level. The Irish and the Italians live in the most undesirable communities, and most of the Portuguese live in E and D communities. Although the E and D communities are low in desirability scale, it has been found that extreme psychopathy is to be expected only at the very lowest level, that is, in the truly slum areas.[2] Once one starts to move up the socioeconomic ladder, psychopathy becomes increasingly inhibited.

The low incidence of psychopathy, coupled with the high rate of psychoneurosis, among the Jews is not difficult to account for. The Jews seem to have acquired a special aptitude for adaptation to a new environment after centuries of migration into unfriendly surroundings. They have even devised special aids, such as the Hebrew Immigrant Aid Society, to smooth the early steps of adaptation for the immigrant, preventing his settling in the worst slums. The desirability level of their communities is higher than those of the Irish, Italians and Negroes. The stresses to which Jews are subjected in this area are not primarily those of frustration of their elementary physical needs, and consequently not such as to arouse psychopathy as a natural reaction. Further, their culture has been one dominated by a strong religion, which restrains them from asocial conduct. For centuries they have offered no military resistance to oppression. "I adjure you that if the government decrees harsh decrees, rebel not against any matter that it imposes upon you" (*Eccles.* VIII, 2). The asocial conduct of the psychopath has become culturally taboo and, as will be noted, the Jew is restrained from alcoholism. Accordingly, the principal outlet for his stress is psychoneurosis. Myerson[6] attributes to the Jew "an apprehensiveness and an emotionality that arose from the conditions of life to which his Christian neighbors subjected him."

One of the interesting findings indicated in Table 9 is the comparatively low rate of psychopathy among the Chinese. The majority of the Chinese considered are subject to at least the same sources of stress as are the Irish and the Italians. They live in one of the densest and most undesirable communities; they are burdened by all the

oppressions of immigrant stress; they suffer from maladjustment resulting from a rural-urban shift, for larger numbers come from rural areas in China; they are deprived of many outlets by the presence of their families in China and by the shortage of Chinese women here. Yet the rate for psychopathy among them is comparatively low. This finding seems to indicate clearly the significance of racial factors in the etiology of mental disorders. Whether, in this case, the factors are biologic we cannot say, but it is clear that the culture of the Chinese has rendered both psychopathy and alcoholism unacceptable as outlets to stress. This rejection of violence is evident in the Chinese religious philosophy, which, like the religion of the Jews, serves to instill a deep respect for the law of the country. Psychoneurosis remains as the primary outlet for stress of the Chinese. Had those rejected for mental deficiency been able to express themselves more fluently, psychoneurosis would probably have been found even oftener. (This error is not involved in the psychopathic or alcoholic groups, for adequate social-service records are available.)

The Negroes have the highest rate for both psychoneurosis and psychopathy. One reason for this may be that the Negroes in this study come from communities of varying densities and economic levels. A further and possibly more significant factor is the intensity and severity of the stress to which many of the Negroes are subjected. Aggressiveness is a natural reaction to physical stress, but when the stress is severe enough the individual is so completely oppressed that any impulse to aggressiveness is itself frustrated. When this happens the individual seldom hopes to overcome oppression and resigns himself to his distress. When he is thus discouraged, the principal outlet for his stress is psychoneurosis. It is probable that many of the Negro psychoneurotics fall into this group.

There is some correlation between the rates of chronic alcoholism (Table 10) and of psychopathy.

TABLE 10. *Differences in Rejection Rates for Chronic Alcoholism in Communities of Different Predominant Nationalities.*

NATIONALITY	REJECTION RATE
	%
Irish	3.0
Negroes	2.2*
Italian	1.2
Portuguese	0.6
Old American	0.4
Jewish	0.2
Chinese	0.0*

*Not community but individual figures.

In both cases, for instance, the Irish, Negroes and Italians, in varying order, are found to be the top three. But the rate for alcoholism among the Irish surpasses that of any other group. This variation cannot be explained in terms of socioeconomic level or population density, for the Chinese, whose community is at least as dense and undesirable as those of the Irish, show an absence of alcoholism. Moreover, there is a marked difference between the Irish and the Italian communities in the rate for alcoholism, although there are no corresponding differences in density and desirability.

Alcohol among the Italians, Portuguese and Chinese is used primarily in the form of wine at mealtime and on festive occasions. It is seldom used in order to drown sorrow or to escape from physical and mental stress. Although wine may occasionally be taken to excess, the wine-drinking people have never been reported to have as much alcoholism as the hard liquor drinking nations of the north.

The Jews and the Chinese are lowest in the rate of alcoholism. The religion and culture of the Jews have restrained them from the social disgrace of drunkenness. The Chinese have not used alcohol as an emotional outlet, because to be drunk or disorderly brings shame on themselves and their families. (No Chinaman has yet been rejected for chronic alcoholism at this station.)

The high rate of alcoholism among the Negroes can be explained on the same basis as the high rate of psychopathy and psychoneurosis. The Negro is severely oppressed by all the types of stress mentioned; his impulse to aggressiveness is often in itself frustrated, and the result is that he is likely to become discouraged and broken. Alcoholism is an obvious outlet for this sort of stress, when alcohol is available.

The high rate of alcoholism among the Irish is less easily explained. It is known that alcohol has long been used freely by the Irish as a means of creating social conviviality after physical and nervous fatigue, and as a medicine, and its use in these ways has long been culturally acceptable. No other nationality in this study, with the possible exception of the Old American, uses alcohol in a manner similar to the Irish. The Old Americans, who are in a relatively secure social position, are subject to little or no abnormal stress and consequently are not in need of alcohol as an emotional outlet. We cannot determine to what extent alcohol would be used among the Old Americans were they under the same stress as the other groups. The Irish are subjected to a sufficient stress to permit an easy extension of their normal use of alcohol.

The rate of mental deficiency among the Chinese, Negroes, Italians and Portuguese (Table 11) is disproportionately high. Our figures are misleading, however, unless they are interpreted in terms of a number of racial and cultural factors.

Probably some of these findings can be attributed to the unavoidable limitations of our psychometric examination. We know that some members of these groups have resented being drafted and

as a result were not motivated to their best performance. Every practicable precaution against malingering is taken, but low motivation is important in borderline cases, and it is probable that

TABLE 11. *Differences in Rejection Rates for Mental Deficiency Found in Communities of Different Nationalities.*

PREDOMINANT NATIONALITY	REJECTION RATE
	%
Chinese	24.5*
Negro	11.7*
Italian	3.9
Portuguese	3.1
Irish	1.2
Jewish	0.9
Old American	0.7

*Not community but individual figures.

many who were rejected might have been accepted as borderline had they been better motivated. Further, although our psychologic tests are designed to measure intelligence or ability to learn, as distinguished from education or information, we cannot claim that this intention is realized in every case. The Chinese and, to a lesser extent, the Negroes and Portuguese seem to have insufficient familiarity with the materials from which some of the tests have been constructed, and this lack of familiarity may often result in an invalid performance.

Possibly the best cultural explanation of these findings is provided by the theory that apparent mental deficiency, in many cases, is merely a reaction to emotional stress. Dollard,[12] in his study of caste and class in southern towns, noted that the frustrated Negro, unable to find any aggressive outlet for his stress, unconsciously assumed an attitude of stupidity. In this way the completely discouraged individual was enabled both to incur revenge and to exempt himself from disagreeable responsibilities. Maslow and Mittelman[13] insist that this apparent stupidity is an unconscious mechanism. They state: "This roundabout and inefficient path is chosen because the individual's fundamental needs have in one fashion or another been frustrated or come into conflict with one another. Give him back his self-esteem and his feeling of security, and his symptoms — whether apparent stupidity or hostility or compulsion — tend to disappear." The Laotian philosophy, as Lin Yutang has reminded us, has taught the Chinese that there is wisdom in "embracing folly."

Our figures concerning the Chinese are not strictly comparable with those of the other groups. It is not true that 24.5 per cent of the Chinese are feeble-minded. What this figure means is that this percentage of the Chinese were judged, in view of their apparently complete inability to understand English, to have insufficient endowment to absorb Army training in the time provided for such purposes.

The low rate of mental deficiency among the Jews is not difficult to explain. Their stress is such as to provoke psychoneurosis. Unlike the Negroes, they are not so severely oppressed that they must resort to apparent stupidity as an exemption. Education has always been venerated by the Jews, since it has been necessary in their preservation under oppression ("Mine anointed are the school children. My prophets are the scholars." — *I Chron.* XVI, 22). Their low rate on failure on mental tests can be attributed partly to their higher education, to the cultural opportunities afforded by their urban background and to their intense motivation to make high scores.

SUMMARY

At the Boston Armed Forces Induction Station the rejection rates for five types of mental disorders among seven different national or racial groups were determined.

The Negroes, Irish and Italians have high rates for psychopathic personality and chronic alcoholism; the Negroes, Chinese, Russian Jews and Portuguese for psychoneurosis; and the Chinese, Negroes, Italians and Portuguese for mental deficiency. The Negroes have high rates for all five types of disorder. The Old Americans have comparatively low rates.

These findings are partly explained in terms of socioeconomic level, population density and the cultural differences of the different nationalities.

This study presents sufficient evidence of cultural differences as etiologic factors in mental disorders to suggest both the need of further investigation in this direction and the possibility of extensive application of mental hygiene.

REFERENCES

1. Bloomberg, W., and Hyde, R. W. Survey of neuropsychiatric work at Boston Induction Station. *Am. J. Psychiat.* **99**:23-28, 1942.
2. Hyde, R. W., and Kingsley, L. V. Studies in medical sociology. I. Relation of mental disorders to community socioeconomic level. *New Eng. J. Med.* **231**:543-548, 1944.
3. *Idem.* Studies in medical sociology. II. Relation of mental disorders to population density. *New Eng. J. Med.* **231**:571-577, 1944.
4. Malzberg, B. *Social and Biological Aspects of Mental Diseases.* 360 pp. Utica, New York: State Hospitals Press, 1940. P. 203.
5. Bailey, P. Contribution to mental pathology of races in United States. *Ment. Hyg.* **6**:370-391, 1922.
6. Myerson, A. Nervousness of the Jew. *Ment. Hyg.* **4**:65-72, 1920.
7. Lenroot, K. F. *Juvenile Delinquency.* 182 pp. Washington, D. C.: Children's Bureau, United States Department of Labor, October, 1929.
8. Glueck, B. Study of 608 admissions to Sing Sing Prison. *Ment. Hyg.* **2**:85-151, 1918.
9. Stearns, A. W. *The Personality of Criminals.* 146 pp. Boston: The Beacon Press, Inc., 1931.
10. Levy, J. Conflict of cultures and children's maladjustment. *Ment. Hyg.* **17**:41-50, 1933.
11. Klineberg, O. *Race Differences.* 367 pp. New York: Harper & Brothers, 1935. P. 254.
12. Dollard, J. *Caste and Class in a Southern Town.* 502 pp. New Haven: Yale University Press, 1937.
13. Maslow, A. H., and Mittelman, B. *Principles of Abnormal Psychology.* 638 pp. New York: Harper & Brothers, 1941. P. 545.

PHYSICAL THERAPY IN WARTIME*

K. G. Hansson, M.D.†

NEW YORK CITY

IN WARTIME most human endeavors are accelerated. This applies especially to medicine, and all the specialties are included. This paper attempts to discuss how physical therapy has "gone to war," and also points out lessons from the war that will undoubtedly influence civilian hospitals in the future. It is a pleasure to testify that it was Dr. Brackett and Dr. Goldthwait, of Boston, who were mainly responsible for the establishment of physical therapy in World War I, and that it was Dr. Granger, of Boston, who represented physical therapy in the Surgeon General's Office during the last war.

During the present war, the Surgeon General has ordered that general and other large hospitals in continental United States be provided with standard equipment for electrotherapy, hydrotherapy and thermotherapy, with gymnasium apparatus and with equipment for research. Most of the American hospitals in Alaska, Australia, Africa and Italy and at other operational bases are similarly equipped. These departments of physical therapy are under the direct supervision of one or more medical officers trained in this field. The aides must have the same training as that required by the American Medical Association, and were commissioned by an act of Congress in February, 1943. The Army has also assigned certain hospitals for specific treatment, such as the Walter Reed General Hospital for amputation cases, the Ashford General Hospital for arthritis and the Fitzsimons General Hospital for rehabilitation.

The amount of work done in a physical-therapy department may be judged from the July, 1943, report from the Lawson General Hospital, where 10,056 treatments were given. The types of cases treated do not differ much from those in civilian life. They are back injuries, painful feet, knee injuries, strains, sprains, dislocations, fractures and burns. Now, however, since combat casualties are arriving, there is an increase in fractures, nerve injuries, burns and wounds of the soft tissue. The treatment of these cases is much the same as that in civilian hospitals, with special emphasis on whirlpool baths, occupational therapy, active exercises and massage.

Physical therapy in the Navy is similar to that in the Army, but owing to ship regulations much of the work is done by more or less trained corpsmen or pharmacists' mates.

* * *

One of the outstanding contributions of the war so far has been the revision of convalescent care; this may be called rehabilitation, reconditioning or streamlined convalescence. The fact is that the uses and abuses of bed rest are being analyzed. It is evident that the increased supply of hospital beds, the development of the profession of nursing and the widespread use of hypnotics and narcotics are largely responsible for the present use of absolute bed rest. It has become familiar to all to see wards full of patients lying flat in bed, absolutely quiet and guarded against moving by nurses. The solid foundations of bed rest as a therapeutic measure, however, are being shaken, and absolute rest is being challenged. The facts that it costs $20,000 to train a pilot and that it is more economical to cure such a patient than to train a new pilot may be the original cause of this revision of convalescence. It seems rational to review some of the factors concerning bed rest, and to describe certain of the physical-therapy measures to be used to discharge a patient in a better general condition than that when he entered the hospital. By discussing the various body systems separately, it may be possible to draw some conclusions concerning rest *versus* activity.

Skeleton. The posture that a patient assumes in bed is physiologically abnormal. A painful neck, an aching back and stiff knees are frequent symptoms of bed rest. Their occurrence can be prevented by the knowledge and application of proper body mechanics. Immobilization produces a negative calcium balance, which in turn may be counteracted by proper ultraviolet radiation every other day, either individually or, as is done at the New York Hospital, in specially built solariums equipped with powerful Finsen carbon arcs. Stiffness of the joints can be prevented by active or passive exercises at prescribed intervals.

Muscular system. The muscles are intended for activity, and when they are deprived of this, they become stiff, lose their tone and may go on to atrophy. Massage eliminates the lactic acid and carbon dioxide responsible for the stiffness, and muscle-setting exercises maintain tone and prevent atrophy.

Circulatory system. The circulatory system is probably the greatest sufferer from complete bed rest. Hyperemia, congestion and edema are frequent. It is less generally realized that constant

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 23, 1944.

†Assistant professor of clinical surgery, Cornell University Medical College; director of physical therapy, Hospital for Special Surgery and New York Hospital.

pressure on the veins in the calves may cause thrombosis, which in turn may be responsible for pulmonary emboli. Autopsies show that 30 per cent of all hospital patients have thrombi in the veins of the calves. In adults who have been in bed two weeks or longer, the incidence reaches 60 per cent. All show necrosis and inflammatory reactions in the calf muscles, which apparently initiate the process. Of the last 300 adult patients autopsied at the New York Hospital, 5 per cent died of pulmonary embolisms secondary to thrombi in the legs. This equals the number of deaths from cancer of the stomach, and the fatalities are considered due to complete bed rest. Such serious circulatory disturbance can be prevented by systematized exercises and changes of position in bed. This regime also maintains an adequate blood pressure and prevents dizziness when getting up.

Gastrointestinal system. The constipation of the bedridden patient is usually accepted as unavoidable, and many people ascribe their chronic constipation to previous confinement in bed. The objectional bedpan is probably a contributory agent. The straining on a bedpan is probably underestimated, the danger of bathroom privileges is overestimated, and the result is that the patient becomes constipated from bed rest. It has been shown that there is no significant difference in the loss of energy from sitting as against that from lying flat in bed. In the Scandinavian countries abdominal massage is much in vogue to counteract constipation. If more abdominal massage were used, permission for sitting up and bathroom privileges were granted oftener and bedpans were less used, constipation from bed rest could be managed better than with the cathartic pill of some patent medicine.

Skin. Irritation of the skin is obvious and receives the immediate attention of the nurse. It has increased in frequency owing to the chemicals used in modern hospital laundries. Skin ulcers and bedsores are often considered the result of poor nursing, but bed rest is equally responsible. It is questionable whether the daily alcohol rub is the best solution, and whether it would not be physiologically sounder to use some fatty-acid application, together with changes in positions, and ultraviolet radiation.

Nervous system. Regarding the nervous system, the mind suffers most from being confined to one room and immobilized in bed. The rules of hospitalization regulate patients' days and nights so that they have no more responsibilities and have much time to feel sorry for themselves. At night, when darkness shuts out most external impressions, painful sensations are increased. Occupational therapy is available to counteract many of the mental reactions of bed rest, and functional occupational therapy is most important to regain active motion.

* * *

In my visits to various reconditioning centers, I have been impressed by this new conception of convalescence, but on closer inspection one finds that the medical officers are handicapped by the lack of trained personnel to carry out these new ideas. The actual work of the convalescent program is usually carried out by men trained only in physical education. They are all eager and enthusiastic, but the realization of these new rational ideas is not without danger. Great discrimination must be used in selecting the patients and the type of exercises to be employed. One gains the impression that the medical departments of the armed services have contributed a valuable advance in medical care, and it is to be hoped that this contribution can be put on a rational basis. Physical therapy has a very important part to play in this convalescent program. It is needless to point out that no radical departure from the rest treatment in tuberculosis, hypertension or comatose patients is advocated but this revision of the traditional hospitalization of patients must be considered in civilian practice. The advantage of the so-called "Kenny treatment" of poliomyelitis is not that it cures more patients than other methods, but that the early application of activities turns out patients in better general health and with better circulation and muscular function than the old immobilization treatment produced.

Physical therapy has many contributions to offer when one considers the immediate necessity for shortening hospitalization, not only in the armed services but also in civilian life. It is high time to bring physical therapy into the wards of civilian hospitals. There has been a tendency to centralize it in a department. This is still necessary in many applications, such as hydrotherapy, mechanotherapy, underwater exercises, electrotherapy and so forth, but the time has come to attempt more active treatment of the bedridden patient. Physical therapy can be utilized to shorten the stay in bed, to counteract many deplorable results of bed rest and to turn out a discharged patient with more adequate circulation, better muscular tone, better posture, a normally functioning gastrointestinal tract, better skin and a mind that is mentally alert instead of depressed.

321 East 42d Street

MEDICAL PROGRESS

PARENTERAL-FLUID THERAPY

II. The Estimation of Losses Incident to Starvation and Dehydration with Acidosis or Alkalosis and the Provision of Repair Therapy*

ALLAN M. BUTLER, M.D.,† AND NATHAN B. TALBOT, M.D.‡

BOSTON

IN THE first part of this review of parenteral-fluid therapy[67] the parenteral provision of the daily maintenance needs was considered. This part deals with the parenteral repair of the losses of water and electrolyte incident to dehydration. For if a patient requiring parenteral therapy has suffered starvation and severe dehydration, the amount and quality of the losses must be estimated, and appropriate repair needs must be provided parenterally *in addition to* the maintenance requirements.

CLINICAL APPRAISAL OF DEHYDRATION

The extent of the dehydration cannot be estimated reliably by any single laboratory procedure.[52] Serial determinations of body weight, blood hemoglobin concentration,[68] red-cell and white-cell counts, and plasma protein[69] and nonprotein nitrogen concentrations may contribute to a retrospective appraisal of the degree of the dehydration and the response to therapy, but even such serial determinations will not provide the pertinent information obtained by a careful history and physical examination and by the continued detailed clinical observation of the patient during therapy.

The history of weight loss, dietary and fluid intake and losses by urine, stool, vomiting, insensible loss, sweating or other routes, together with the symptoms, indicate the nature and extent of the starvation and fluid loss. In addition, they suggest the probability of acidosis or alkalosis being associated with the dehydration.[52, 70, 71]

By physical examination the clinical appraisal of the weight loss, tongue, mucous membranes, skin turgor, hydration of the eye and periocular tissue, heart action, peripheral circulation, fecal masses in the bowel, stools, urine volume and concentration and, in the infant, the fontanelle further define the extent of the dehydration and starvation. Muscular hypertonicity, hyperactive reflexes, a positive Chvostek or Trousseau sign or carpopedal spasm suggests alkalosis. Deep and exaggerated respirations confirm the probability of metabolic acidosis[52, 70–74] or primary stimulation of the respiratory center with respiratory alkalosis.[52, 70, 71, 73–76] In the absence of extreme shock or emphysema, shallow and irregular respirations support the probability of alkalosis.[52, 70, 71, 77, 78] Great caution must be taken in using the urinary pH as an index of acidosis or alkalosis. Renal infection may render the urine alkaline in acidosis. In the dehydration of alkalosis the urine may be acid if the cation or sodium concentration of the plasma is below normal, as not infrequently occurs.[70, 78]

Adequate nurse's notes detailing intake and output and signs and symptoms and frequent reexamination of the patient by the physician reveal much concerning the response to therapy.

In the early stages of appraisal and therapy, readily obtainable clinical information utilized with reasonable clinical judgment is far more valuable than the usually available laboratory determinations. Too often these latter in being substituted for clinical acumen provide little or misinterpreted information. For example, as discussed later and illustrated in Figure 1, a patient with an abnormally low plasma or blood carbon dioxide content may be suffering either from a metabolic acidosis — as in diarrhea or diabetic coma — or from a respiratory alkalosis — as in the hyperpnea of hysteria or encephalitis.[52, 70, 71, 73–75, 77] As parenteral therapy proceeds, however, certain laboratory analyses, as discussed in the last section below, are guides essential to the provision of the best therapy.

Ordinarily, most of the weight loss during acute dehydration with starvation is due to loss of body water. Approximately half the loss comes from the extracellular fluids containing Na^+, Cl^- and HCO_3^-, and half from the intracellular fluids containing K^+, Mg^{++}, HPO_4^{--}, SO_4^{--} and protein.[71, 79–84] A loss of between 8 and 12 per cent of the body weight represents significant dehydration. Hence the extracellular and intracellular losses may be estimated, as subsequently outlined in Table I.

It is interesting that a relatively large intracellular fluid loss occurs following hemorrhage.[85]

Rarely, when dehydration occurs at an extremely rapid rate with loss of the extracellular electrolytes Na^+ and Cl^-, — as occurs in a hot box or under anesthesia in a hot operating room or by loss of interstitial fluid while ingesting water, — the plasma volume may be reduced so rapidly that circulatory collapse occurs before marked generalized dehydration has an opportunity to develop.[69, 80, 86]

EXTRACELLULAR LOSSES AND REPAIR

Qualitatively, the extracellular losses vary with the route of loss.[70, 71, 87–89] For example, in vomiting

*From the Children's Medical Service, Massachusetts General Hospital, and the Department of Pediatrics, Harvard Medical School.

†Chief of the Children's Medical Service, Massachusetts General Hospital, and associate professor of pediatrics, Harvard Medical School.

‡Assistant physician, Children's Medical Service, Massachusetts General Hospital, and associate in pediatrics, Harvard Medical School.

there is a greater loss of Cl^- than of Na^+, with a resultant tendency to alkalosis.[77, 90] The alkalosis is then partially compensated by the excretion of Na^+ and K^+ with HCO_3^- in an alkaline urine.[91]

organic and organic acid catabolites and a diminution in the renal excretion of cations (bases) as

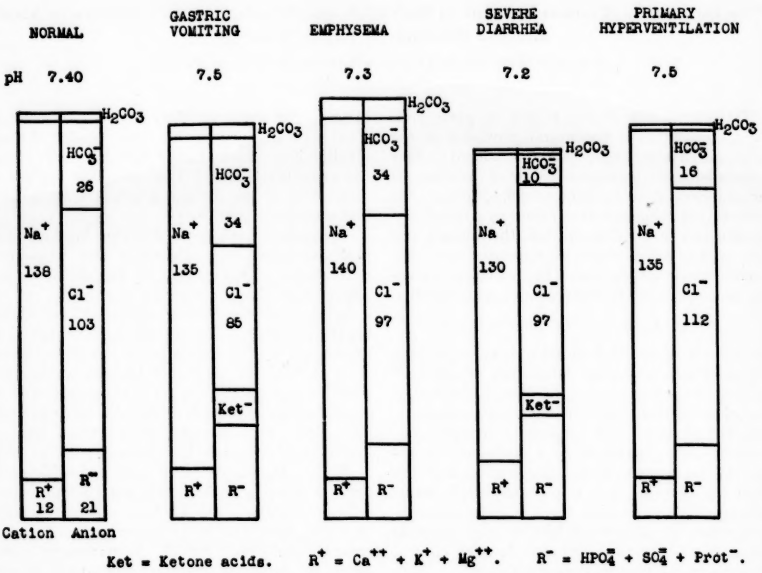

FIGURE 1. *Diagrammatic Representation (according to Gamble) of the Electrolyte Composition of the Plasma of a Normal Subject, a Patient with the Metabolic Alkalosis of Gastric Vomiting, a Patient with the Respiratory Acidosis of Asthma, a Patient with the Metabolic Acidosis of Severe Diarrhea and a Patient with the Respiratory Alkalosis of Hysterical Hyperventilation.*

The numerical values for Na, HCO_3 and Cl represent milliequivalents per liter. The sums of other cations and anions are given merely to show their relative order of magnitude and direction of change in concentration. Similarly the undissociated mols of carbonic acid are diagrammed roughly to indicate the direction of change. The reaction (pH) is proportional to the ratio of the HCO_3 to the carbonic acid.[53, 70, 71]

TABLE 1. *Calculations for Approximating the Extracellular Parenteral Needs, Over and Above the Maintenance Needs, of Dehydrated Acidotic Patients.*

CONSIDERATION	5-KG. INFANT	60-KG. ADULT
Fluid loss:		
Weight before dehydration	5000 gm.	60000 gm.
Weight after dehydration	4400 gm.	54000 gm.
Approximate total fluid loss	600 cc.	6000 cc.
Extracellular loss = half total loss	300 cc.	3000 cc.
Intracellular loss = half total loss	300 cc.	3000 cc.
Provision of repair needs:		
One part M/7 sodium bicarbonate* + two parts physiologic saline solution for extracellular loss and acidosis	300 cc.	3000 cc.
Serum for protein depletion†	100 cc.	800 cc.
Whole blood for hemoglobin and protein depletion‡	100 cc.	500 cc.

*Or M/7 sodium lactate.

†To be given if the serum protein level is low before or during parenteral therapy.

‡To be given if the red-cell count or hemoglobin level and serum protein level are low before or during parenteral therapy.

As the dehydration progresses the renal function is impaired,[92, 93] with a resultant retention of inorganic and organic acid catabolites and a diminution in the renal excretion of cations (bases) as bicarbonates.[70, 78] In diarrhea two factors predispose to acidosis. First, there is a greater loss in diarrheal stools of sodium and other cations (bases) than of chloride and other anions (acids).[94, 95] Second, the impaired renal function incident to the dehydration results in the retention of acid catabolites.[70, 71, 87, 88, 96] Starvation ketosis tends to develop in both the alkalotic dehydration of vomiting and the acidotic dehydration of diarrhea.

Diagrammatic visualization of the disturbances in the balance of cations (bases) and anions (acids) greatly facilitates comprehension of the pathologic physiology of the extracellular fluids.[71] Utilization of unrelated units of concentration, such as milligrams per 100 cc. of chloride and volumes per cent of carbon dioxide for serum and grams of sodium chloride per 100 cc. for physiologic saline solution, makes such visualization impossible and renders thinking difficult. For example, are the Na^+ and Cl^- concentrations of a 0.85 per cent solu-

tion of sodium chloride higher or lower than the normal serum sodium and chloride concentrations of 322 and 365 mg. per 100 cc. respectively?* Or, if a 0.85 per cent solution of sodium chloride is infused fairly rapidly into a dehydrated patient whose kidneys are not functioning adequately, as indicated by an elevated nonprotein nitrogen, will the serum Cl^- level tend to be elevated or lowered? And if the serum Cl^- level is lowered or elevated by 35 mg. per 100 cc., by how many volumes per cent will the carbon dioxide tend to be changed? Perhaps to answer this, one would need to know the effect of the infused saline on the serum Na^+ concentration. These, of course, are questions that everyone can answer readily, because one could hardly use physiologic saline solution parenterally without knowing the answers. But the answers are readily given because, instead of the difficultly integrated units of concentration used above, a single unit of chemical equivalents is generally used in expressing the concentrations of electrolytes in body fluids. The utilization of chemical equivalents as the unit of concentration is logical, because the demand of electroneutrality of the body fluids prescribes an equality or balance of the sum of the electropositive ions (cations) and the sum of the electronegative ions (anions). This unit therefore permits visualization and appraisal of the disturbances in the balance of cations (bases) and anions (acids) in which one is clinically interested. Custom and the order of magnitude of these concentrations in body fluids render the milliequivalent† per liter of solution or per liter of water a convenient and accepted unit of concentration in clinical medicine, as evidenced by all the references given in this review. In considering the equilibrium of electrolytes in the different compartments of body fluids, concentrations expressed as milliequivalents per liter of water are preferable, but the more easily determined milliequivalents per liter of solution suffice for considerations of parenteral fluid therapy.

The accepted normal plasma concentrations in milliequivalents per liter of plasma are as follows:

Cations		Anions	
Na	138	HCO_3	26
K	5	Cl	103
Ca	5	HPO_4	2
Mg	2	SO_4	1
		Organic acid	2
		Protein	16
Total	150	Total	150

The carbon dioxide dissolved as undissociated carbonic acid is normally 1.3 millimoles per liter. As the total carbon dioxide determined in the clinical laboratory is the sum of this dissolved carbon dioxide and the HCO_3^-, the normal total plasma carbon dioxide equals 1.3 plus 26, or approximately 27 millimoles per liter.

Physiologic saline (0.85 per cent sodium chloride) solution contains 145 milliequiv. of Na^+ and 145 milliequiv. of Cl^- per liter.

Using the milliequivalent one can readily appreciate, as shown by the diagrams in Figures 1 and 2, that the Cl^- concentration of physiologic saline solution is appreciably higher than that of normal serum. Therefore, the infusion of such saline solution tends to elevate the serum Cl^- level. This of course tends to lower the HCO_3^- and thus the total carbon dioxide level, a rise of 10 milliequiv. Cl^- tending to effect a 10-milliequiv. lowering of the HCO_3^-. Since the normal HCO_3^- concentration is but 26 milliequiv. per liter, this is a significant reduction. Such an infusion of physiologic saline solution, however, has but little effect on the serum Na^+ concentration. Since the milliequivalent makes all this clear, it is odd that physicians have often resented rather than welcomed its use.

Gamble's[97] graphic presentation of the anatomy and vicissitudes of the extracellular fluids[71, 88] profusely illustrates how the milliequivalent facilitates the clinical appraisal of a patient's status with respect to cation-anion equilibrium, — that is, acidosis and alkalosis, — and thus simplifies clinical thought concerning electrolyte and water metabolism.

Such graphic presentation of the composition of normal plasma and of the plasmas of patients suffering from the dehydration, starvation and metabolic alkalosis of gastric vomiting, from the respiratory acidosis of asthma, from the dehydration, starvation and metabolic acidosis of severe diarrhea and from the respiratory alkalosis of primary hyperventilation is presented in Figure 1. Figure 2 similarly presents the composition of physiologic saline solution, of 1/7 molar sodium bicarbonate solution

*The custom of expressing plasma Cl concentrations as milligrams of sodium chloride per 100 cc. is, of course, illogical, since the Na and Cl concentrations of plasma are not equal.

†An equivalent is the weight of an ion which, in neutralization reactions, is equivalent to 1 gram-atom of hydrogen. Thus, the number of milliequivalents per liter is equal to the milligrams per 100 cc. times ten divided by the equivalent weight, which, in turn, is the atomic weight divided by the valence. For example,

$$322 \text{ mg. sodium per 100 cc.} = \frac{322 \times 10}{23} = 140 \text{ milliequiv. Na per liter.}$$

$$365 \text{ mg. chloride per 100 cc.} = \frac{365 \times 10}{35.5} = 103 \text{ milliequiv. Cl per liter.}$$

$$10 \text{ mg. calcium per 100 cc.} = \frac{10 \times 10}{20} = 5 \text{ milliequiv. Ca per liter.}$$

$$60 \text{ vol. per cent carbon dioxide} = \frac{60 \times 10}{22.4} = 27 \text{ millimoles carbon dioxide}$$

per liter, where 22.4 equals the liters of carbon dioxide that at 0°C. and 1 atmosphere of pressure contain 1 mol of carbon dioxide. In normal plasma, in which the ratio of HCO_3 to H_2CO_3 is 20:1, 27 mm. of carbon dioxide per liter is equal to 1.3 mols of carbonic acid plus 25.7 milliequiv. of HCO_3 per liter. Therefore, the following approximation satisfies clinical purposes:

$$\frac{\text{Vol. per cent carbon dioxide}}{2.3} = \text{milliequivalents } HCO_3 \text{ per liter.}$$

and of a mixture consisting of two parts of the former and one of the latter.

In Figure 1, the diagram of the plasma of a patient with gastric vomiting and excessive loss of chloride shows an abnormally low plasma chloride concentration. Ketone acids, which have accumulated as a result of the starvation, partially replace the loss in Cl^-. The HCO_3^- has increased to balance the Na^+ left uncovered by the Cl^- deficit. The history of gastric vomiting and the resulting elevation in HCO_3^- concentration above normal indicates a metabolic alkalosis. But it is important to note that without the history and physical findings the change in HCO_3^- concentration, as measured by the total carbon dioxide, could not establish such a diagnosis. Thus, although the plasma of a patient with emphysema (Fig. 1) had a similar increase in HCO_3^- and lowering of Cl^-,[70, 71, 73, 98, 99] the latter had an acidosis not an alkalosis. The determination of the serum pH, however, permits this differentiation by chemical means alone.

To treat the case of gastric vomiting, the infusion of 0.85 per cent saline solution, which contains no HCO_3^- and approximately one and a half times more Cl^- than plasma (Fig. 2), tends to increase the low plasma Cl^-, to decrease the elevated plasma HCO_3^- and thus to correct the hypochloremia and alkalosis. The simultaneous infusion of 5 or 10 per cent glucose limits the starvation and reduces the ketosis. Thus, 5 or 10 per cent dextrose in 0.85 per cent saline solution provides an initial parenteral-fluid therapy that is almost ideal for correcting the dehydration and disturbed plasma and extracellular fluid concentrations resulting from gastric vomiting.[52, 70, 71, 77, 87, 90, 100] The choice between 5 and 10 per cent dextrose depends on the amount of solution to be infused. In moderate dehydration, in which the rate of infusion is relatively slow and the total amount moderate, 10 per cent is required to meet the caloric requirements specified for maintenance needs, as noted in the previous article.[67] However, in severe dehydration, in which a more rapid initial rate of infusion is indicated to repair the dehydration, the initial use of 5 rather than 10 per cent dextrose in saline solution appears preferable to avoid excessive hyperglycemia and glycosuria. The greater volume of fluid administered under such conditions of dehydration offsets the diminution in concentration.

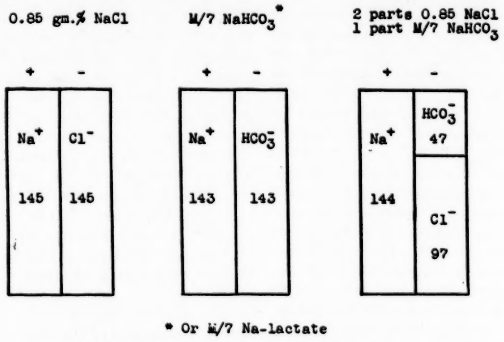

FIGURE 2. *Diagrammatic Representation of the Electrolyte Composition of Physiologic Saline Solution, M/7 Sodium Bicarbonate Solution and a Mixture of Two Parts of the Former and One Part of the Latter. The figures represent milliequivalents per liter.*

The foregoing considerations indicate that the lack of HCO_3^- and the hypertonicity of Cl^- in physiologic saline solution relative to the Cl^- concentration of normal plasma (Figs. 1 and 2) render physiologic saline solution inappropriate as the initial parenteral therapy for correcting the disturbed plasma and extracellular fluid concentrations resulting from dehydration and acidosis. Inspection of the first and fourth diagrams in Figure 1 and the first diagram in Figure 2 should make this clear.

There is ample evidence[87, 89, 101–103] that the infusion of 0.85 per cent saline solution in an acidotic dehydrated patient whose renal function is impaired by the dehydration, as evidenced by an elevated nonprotein nitrogen and other abnormal serum concentrations, may raise the plasma Cl^- above normal and thus prevent increase in the HCO_3^- and alleviation of the acidosis and hyperpnea. Before the

days when sterile sodium bicarbonate and sodium lactate solutions[104] were available, 10 per cent dextrose was added to the physiologic saline solution to so increase blood flow and improve renal function that the excess Cl^- could be excreted promptly.[88, 95] The resulting increase in urine volume favored the urinary excretion of Cl^-, nonprotein nitrogen and other catabolites and the acidosis was ultimately corrected. Fortunately, sterile solutions of sodium bicarbonate or sodium lactate are readily available today. Therefore physiologic saline solution may be so diluted with these solutions that its hypertonicity in Cl^- is corrected and efficient hydration of the acidotic patient may be accomplished without delay in correcting the acidosis and hyperpnea. For example, the third diagram in Figure 2 depicts the concentrations obtained by diluting two parts of 0.85 per cent saline solution with one part of 1/7 molar sodium bicarbonate solution. Because this mixture has an HCO_3^- content almost double that of normal plasma, — that is, 48 milliequiv. per liter, — its infusion to a dehydrated acidotic patient with a low plasma HCO_3^- level and pH (fourth diagram Fig. 1) elevates the lowered plasma and extracellular bicarbonate and thus tends to correct the acidosis. At the same time, because the Na^+ and Cl^- concentrations of this mixture approximate those of normal plasma, it favors the restoration of normal serum Na^+ and Cl^- concentrations while repairing the deficit of extracellular electrolytes. One-seventh molar sodium lactate solution may usually be substituted for the $NaHCO_3$ solution, since the lactate ion appears to be oxidized to HCO_3^- rapidly enough to meet the needs and has the possible advantage of being easy to prepare and nonirritating when given subcutaneously.[104] A greater dilution of physiologic saline solution by bicarbonate or lactate does not appear either necessary or desirable.

The calculation of the bicarbonate requirement, as sometimes done from the plasma carbon dioxide* and weight of the patient,[89, 104, 105] involves the assumption that the bicarbonate contents of extracellular and intracellular fluids are equal. Since it has been shown that no such equality exists,[106, 107] the calculation may involve a 50 per cent error and therefore is hardly worth while. Moreover, the amount of molar sodium bicarbonate that results in a given effect on the serum carbon dioxide has been shown to vary in different patients.[105] Physiologically it appears sounder to appraise the need of bicarbonate by careful clinical appraisal of the metabolic disturbance and respirations as indicated by the history and physical findings.

In appraising acidosis by hyperpnea it should be remembered that hyperpnea may be of central-nervous-system, not metabolic, origin. Primary hyperventilation of such origin, although resulting in a diminished total plasma or blood carbon dioxide, is associated with an alkalosis, not an acidosis.[52, 70, 71, 73–77] The fifth diagram in Figure 1 depicts the plasma of a patient with primary hyperpnea and hence respiratory alkalosis. The HCO_3^- is diminished just as in the patient with the metabolic acidosis of diarrhea, but the pH is elevated and the patient is suffering from an alkalosis. This limitation in the diagnostic information provided by such a carbon dioxide determination is clearly illustrated by the diagrams of Figure 1. The second and third demonstrate that there can be either an alkalosis or an acidosis with an elevated HCO_3^- or total carbon dioxide. The fourth and fifth show that either an alkalosis or acidosis may be accompanied by a low HCO_3^- or total carbon dioxide. Similarly it should be noted that an alkalosis may be present with either a diminished or elevated serum Cl^-, as illustrated in the second and fifth diagrams. The significance of analysis of carbon dioxide or Cl^- depends on a proper correlation of the history and physical findings.

If the metabolic disturbance is a type that predisposes to acidosis, — for example, diarrhea or diabetic coma, — the degree of hyperpnea provides an index of the severity of the acidosis except in the premature, the newborn or the patient in shock.[52, 72] Both the dehydration and acidosis are corrected by the infusion of a mixture of one part 1/7 molar sodium bicarbonate or lactate and two parts 0.85 per cent saline solution at the rate appropriate for hydration of the patient concerned — in other words, at the rate appropriate for the infusion of physiologic saline solution. The amount of this mixture infused is determined by the duration of the hyperpnea. Usually after one to two hours, when the gross hyperpnea has abated, physiologic saline solution may be substituted for the mixture of alkali and saline solution, since at such time the acidosis is no longer extreme and the extracellular hydration has so improved the blood flow and renal function as to permit the selective renal excretion of Cl^- above that of Na^+ and thus the elimination of the excess Cl^- of the saline solution.

The actual manner of estimating the parenteral extracellular repair therapy for an infant and for an adult suffering from acute nutritional failure with diarrhea, dehydration, acidosis and inability to take food and fluids orally is illustrated by the data of Table 1. The indicated repair therapy is of course provided in addition to the required maintenance needs, as stated in the previous article.[67]

As already mentioned, the extracellular loss approximates one half the total weight loss or from 4 to 6 per cent of the patient's weight. The extracellular repair needs are easily provided by the intravenous or subcutaneous administration of

*Assuming that total plasma carbon dioxide per liter times 19/20 equals body fluid HCO_3 per liter and that liters of body fluid equal kilograms body weight times 0.70.

the saline and bicarbonate or lactate solutions. The intravenous administration is usually preferable because it results in less discomfort to the patient than administration by clysis and permits giving with the saline and sodium bicarbonate or lactate solutions the 5 or 10 per cent dextrose that is needed to provide the calories essential for the maintenance requirements.* In considering the administration of dextrose to the dehydrated acidotic patient, just as with the alkalotic one, 5 per cent dextrose appears preferable to 10 per cent in the initial parenteral therapy because the desirable rate of infusion in the initial phase of such therapy exceeds that at which 10 per cent dextrose can be administered without causing excessive hyperglycemia and glycosuria.

The application of these general principles to the initial parenteral therapy of the patient in diabetic coma is apparent. Because the literature is large and the issues somewhat confused, the parenteral therapy of such patients will be considered in a separate review of the therapy of diabetic coma.

Intracellular Losses and Repair

Although the quantitative importance of intracellular losses incident to dehydration is evident,[71, 79–84] little is known about their qualitative differences according to the manner of the dehydration and the occurrence of intracellular alkalosis or acidosis.[106, 109]

Such transfusions of whole blood or plasma as are specified in Table 1 are given primarily to sustain red-cell and plasma volumes and plasma protein concentration. Some recent evidence indicates that plasma transfusions may be less effective in maintaining blood and plasma volumes than are whole-blood transfusions[53–55]; however, they provide some cellular nourishment, although the amount so provided is small. Recent observations concerning carbonic anhydrase[110] suggest another advantage of whole blood over plasma. Carbonic anhydrase is an enzyme that accelerates the splitting of carbonic acid to form carbon dioxide and water. The enzyme is present in red cells[111] and is inhibited by serum.[112] The low concentrations of carbonic anhydrase observed in premature and newborn infants[113] increase following transfusions of adult blood.[113] Thus it has been suggested that whole-blood transfusions have a particular role in treating the acidosis and cyanosis of the newborn.[113]

Ringer's solution contains so few of the intracellular electrolytes that its administration accomplishes little more than giving an unwarranted feeling of satisfaction to the physician and causing expense to the hospital or patient. The provision of amino acids is included in the recommended maintenance therapy given in the first article.[67] The amounts specified barely cover normal maintenance requirements. In extremely depleted patients or patients sustaining severe nitrogen losses incident to burns[7] or shock,[6, 8–10] larger amounts of amino acids may be indicated.

But the addition of such intracellular parenteral therapy to the routine extracellular parenteral solutions does not provide the PO_4^{--}, K^+, Mg^{++} and Ca^{++} that have been lost by these depleted patients and that are essential to a resumption of normal cellular metabolism. Therefore, until the present limitations in providing these substances parenterally are overcome, it is important to start oral feedings as soon as this can be accomplished without nausea or diarrhea.[52, 89] Since adequate dextrose, extracellular constituents and intracellular crystalline enzymes or vitamins can be given parenterally, the oral feedings should provide readily digested foods, containing nitrogen, potassium, phosphate, magnesium and calcium. Beef broth, diluted milk and properly flavored amino acid preparations, if not nauseating, are suitable.

An acute nutritional disturbance, particularly in infants, is not infrequently accompanied by a diminution in gastric acidity and invasion of colon bacilli into the stomach. The dilution and acidification of fat-free milk with a lactate buffer (pH 3) has been advocated as a means of facilitating acid gastric digestion and restoring normal gastric acidity when milk feedings are started.[114] Whether or not the sodium content of this buffer makes it superior to lactic acid appears to depend on the patient's need for extracellular base. Attention has recently been called to the possible danger of overacidification.[115] The addition of ascorbic acid and members of the vitamin B complex to the oral feedings of depleted patients seems desirable.

It is frequently advantageous to start small oral feedings for intracellular repair before the parenteral fluid therapy is discontinued. In so doing some of the essential intracellular nutrients can be provided early with a minimal demand on gastrointestinal function. As the patient demonstrates an ability to handle the oral feedings, they are increased in amount and the parenteral fluids are eliminated.

Checking the State of the Patient

Although careful observation of fluid intake, urine volume, number and volume of stools, respirations, pulse, temperature (including the extremities) and state of hydration by physical examination is essential and invaluable,[82] adequate appraisal of the state of a previously depleted patient who has been nourished only by parenteral fluids for longer than twenty-four hours is difficult without the aid of chemical analyses of the blood. This is particularly true in the presence of continuing vomiting, diarrhea or the loss of gastric and intestinal juices by other routes.

Determination of whole-blood hemoglobin and the serum concentration of protein indicates the

*Although 5 per cent dextrose may be given subcutaneously in the dehydrated patient it not only may be absorbed very slowly but also may in the process of absorption remove extracellular fluid.[89, 108]

need of whole blood or serum, initially or in the course of parenteral-fluid therapy. Comparison of serial or daily hemoglobin and protein values reveals the trend in the patient's water balance and need of fluid.[68, 69] The relative adequacy of renal circulation and function may be appraised by determining the nonprotein nitrogen concentration. The presence of chloride depletion with increased serum HCO_3^- concentration, alkalosis and the need of physiologic saline solution, or the presence of base deficit with a decreased serum HCO_3^- level, acidosis and the need of the combination of sodium bicarbonate (or lactate) and saline solution, may be determined initially or checked during therapy by analyses of the serum concentrations of chloride and either sodium or carbon dioxide. However, as already mentioned, a careful interpretation of the history and clinical findings is necessary before the carbon dioxide content of the serum can be used as an index of alkalosis or acidosis. Indeed, a clinical appraisal that permits interpretation of the carbon dioxide concentration usually means that the actual determination of the carbon dioxide contributes but confirmatory information. The presence of acidosis or alkalosis may be definitely established by determining the serum or whole-blood pH.

The amounts of blood or serum required for these analyses are as follows: hemoglobin, 0.02 cc. of whole blood[116]; serum protein, 0.02 cc.[117]; nonprotein nitrogen, 0.1 cc. of whole blood or serum[118]; serum chloride 0.5 cc.[119]; serum sodium, 0.5 cc.[120]; serum carbon dioxide, 0.5 cc.[121]; and pH, 0.2 cc.[122]

Summary

The parenteral therapy of the patient unable to take fluids or food by mouth has been reviewed. The first part of this review outlined the estimation of maintenance requirements and the provision of maintenance therapy under the separate categories of water, sodium chloride, nitrogen and calories. This, the second, part considers the estimation of the losses incident to starvation and dehydration and the provision of repair therapy. It specifically deals with the clinical appraisal of the dehydration and the accompanying acidosis or alkalosis; extracellular losses and their repair; intracellular losses and repair; and checking the state of the patient and his needs by blood analyses.

The importance of providing the therapy described under all these categories is emphasized. It is hoped that this manner of review provides physiologic concepts and therapeutic measures that may be integrated by the physician to meet the needs of each patient.

The data tabulated under each category are applicable to the parenteral therapy of infants, children and adults. The requirements of sodium chloride for maintenance and for repair are reviewed separately to emphasize their different orders of magnitude. Appreciation of this difference should avoid oversalting the patient requiring only maintenance therapy and undersalting the patient requiring extensive extracellular repair therapy. The possible need of providing 10 to 15 per cent dextrose in maintenance parenteral therapy where relatively moderate total volumes of solution are infused at a slow rate is indicated. On the other hand, where a larger volume of repair solution is being rapidly infused in the initial therapy of severe dehydration, a concentration of 5 per cent dextrose in the parenteral fluid appears to provide a total amount adequate to meet the caloric requirements. The suitability of using 0.85 per cent saline solution in the parenteral therapy of the dehydrated alkalotic patient is described. The inappropriateness of such a solution in the initial parenteral therapy of the dehydrated acidotic patient and the desirability of substituting a mixture of one part 1/7 molar sodium lactate or bicarbonate solution and two parts physiologic saline solution are emphasized. The simplification of thought concerning disturbances in water and electrolyte balance provided by utilization of the milliequivalent as the unit of concentration is illustrated.

Attention is called to the importance of intracellular losses in dehydration and starvation and to the inadequacy of present-day parenteral therapy to repair such losses. The administration of appropriate food orally early during the course of therapy is emphasized.

References

67. Butler, A. M., and Talbot, N. B. Parenteral fluid therapy. I. Estimation and provision of daily maintenance requirements. *New Eng. J. Med.* **231**:585-590, 1944.
68. Seaman, B. W., and Ponder, E. Estimation and control of postoperative dehydration, with aid of hemoglobin and plasma protein determinations. *J. Clin. Investigation* **22**:673-685, 1943.
69. Brown, H. R., Jr., Clark, W. F., Jones, N., Walther, J., and Warren, S. L. Relationship of dehydration and overhydration of blood plasma to collapse in management of artificial fever therapy. *J. Clin. Investigation* **22**:471-485, 1943.
70. Peters, J. P., and Van Slyke, D. D. Carbonic acid and acid-base balance. In *Quantitative Clinical Chemistry*. Vol. I. Interpretations. 1265 pp. Baltimore: Williams & Wilkins Company, 1932. Pp. 868-1018.
71. Gamble, J. L. *Chemical Anatomy, Physiology and Pathology of Extracellular Fluid: A lecture syllabus*. Department of Pediatrics, Harvard Medical School, 1942.
72. Howland, J., and Marriott, W. M. Acidosis occurring with diarrhea. *Am. J. Dis. Child.* **11**:308-325, 1916.
73. Peters, J. P., Bulger, H. A., Eisenman, A. J., and Lee, C. Total acid-base equilibrium of plasma in health and disease. IV. Effects of stasis, exercise, hyperpnea, and anoxemia; and causes of tetany. *J. Biol. Chem.* **67**:175-218, 1926.
74. Shock, N. W., and Hastings, A. B. Studies of acid-base balance of blood. IV. Characterization and interpretation of displacement of acid-base balance. *J. Biol. Chem.* **112**: 239-262, 1935.
75. Harrop, G. A., and Loeb, R. F. Uncompensated alkalosis in encephalitis. *J. A. M. A.* **81**:452-454, 1923.
76. Talbot, J. H., Cobb, S., Combs, F. S., Cohen, M. E., and Consolazio, W. V. Acid-base balance of blood in patient with hysterical hyperventilation. *Arch. Neurol. & Psychiat.* **39**:973-987, 1938.
77. MacCullum, W. G., Lintz, J., Vermilye, H. N., Liggett, T. H., and Boas, E. Effect of pyloric obstruction in relation to gastric tetany. *Bull. Johns Hopkins Hosp.* **31**:1-7, 1920.
78. Hartmann, A. F., and Smyth, F. S. Chemical changes in body occurring as result of vomiting. *Am. J. Dis. Child.* **32**:1-28, 1926.
79. Butler, A. M., McKhann, C. F., and Gamble, J. L. Intracellular fluid loss in diarrheal disease. *J. Pediat.* **3**:84-92, 1933.
80. Nadal, J. W., Pedersen, S., and Maddock, W. G. Comparison between dehydration from salt loss and from water deprivation. *J. Clin. Investigation* **20**:691-703, 1941.
81. Mellors, R. C., Muntwyler, E., and Mautz, F. R. Electrolyte and water exchange between skeletal muscle and plasma in dog following acute and prolonged extracellular electrolyte loss. *J. Biol. Chem.* **144**:773-784, 1942.
82. Elkinton, J. R., and Taffel, M. Prolonged water deprivation in dog. *J. Clin. Investigation* **21**:787-794, 1942.

83. Elkinton, J. R., and Winkler, A. W. Transfers of intracellular potassium in experimental dehydration. *J. Clin. Investigation* **23**: 93-101, 1944.
84. Butler, A. M., and Gamble, J. L. Utilization of sea water by castaways. Final Report. Contract OEMcmr-180. Washington, D. C., 1944.
85. Stewart, J. D., and Rourke, G. M. Intracellular fluid loss in hemorrhage. *J. Clin. Investigation* **15**:697-702, 1936.
86. Adolph, E. F., Rahn, H., Gosselin, R. E., Goddard, D. R., Brown, A. H., Kelly, J. J., Wolf, A. V., Wills, J. H., and Rothstein, A. Water losses, circulatory and temperature changes during desert dehydration. Interim Reports 1, 2, 4 and 9. Contract OEMcmr-206. Washington, D. C., 1943.
87. Hartmann, A. F. Chemical changes occurring in body as result of certain diseases. I. Effect of diarrhea, vomiting, dehydration and oliguria on acid-base balance of plasma in infants with mastoiditis. *Am. J. Dis. Child.* **35**:557-575, 1928.
88. Gamble, J. L. Extracellular fluid: extracellular fluid and its vicissitudes. *Bull. Johns Hopkins Hosp.* **61**:151-173, 1937.
89. Darrow, D. C. Treatment of dehydration acidosis and alkalosis. *J. A. M. A.* **114**:655-660, 1940.
90. Gamble, J. L., and Ross, S. G. Factors in dehydration following pyloric obstruction. *J. Clin. Investigation* **1**:403-423, 1925.
91. Gamble, J. L. Carbonic acid and bicarbonate in urine. *J. Biol. Chem.* **51**:295-310, 1922.
92. Schoenthal, L., Lurie, D., and Kelly, M. Urea clearance in normal and in dehydrated infants. *Am. J. Dis. Child.* **45**:41-53, 1933.
93. Young, W. F., and McCance, R. A. Secretion of urine by dehydrated and normal infants. *Arch. Dis. Childhood* **17**:65-81, 1942.
94. Holt, L. E., Courtney, A. M., and Fales, H. L. Chemical composition of diarrheal as compared with normal stools in infants. *Am. J. Dis. Child.* **9**:213-224, 1915.
95. Hoag, A. L., and Marples, E. Acid-base status in dehydration accompanying diarrhea in infants: effect of treatment with parenteral fluids. *Am. J. Dis. Child.* **42**:291-313, 1931.
96. Hamilton, B., Kajdi, L., and Meeker, D. Acidosis of acute diarrhea in infancy. *Am. J. Dis. Child.* **38**:314-322, 1929.
97. Gamble, J. L., Ross, S. G., and Tisdall, F. F. Metabolism of fixed base during fasting. *J. Biol. Chem.* **57**:633-695, 1923.
98. Scott, R. W. Observations on pathologic physiology of chronic pulmonary emphysema. *Arch. Int. Med.* **26**:544-560, 1920.
99. Blalock, H., Harrison, T. R., and Wilson, C. P. Partial tracheal obstruction: experimental study in effects on circulation and respiration of morphinized dogs. *Arch. Surg.* **13**:81-95, 1926.
100. Drake, T. G. H., Marsh, P., and Gamble, J. L. Alkalosis of vomiting and acidosis of advanced renal disease. *Am. J. Dis. Child.* **40**: 705-717, 1930.
101. Marriott, W. M., and Hartmann, A. F. Newer aspects of acidosis. *J. A. M. A.* **91**:1675-1679, 1928.
102. Cooper, E. D. Studies in gastro-enteritis. *Arch. Dis. Childhood* **12**:339-368, 1937.
103. MacLachlan, E., Rourke, M. G., and Butler, A. M. Unpublished data (Infants' and Children's hospitals and Massachusetts General Hospital, Boston).
104. Hartmann, A. F., and Senn, M. J. E. Studies in metabolism of sodium r-lactate. I. Response of normal human subjects to intravenous injection of sodium r-lactate. II. Response of human subjects with acidosis to intravenous injection of sodium r-lactate. *J. Clin. Investigation* **11**:327-335 and 337-344, 1932.
105. Palmer, W. W., and Van Slyke, D. D. Studies of acidosis: IX. Relationship between alkali retention and alkali reserve in normal and pathological individuals. *J. Biol. Chem.* **32**:499-507, 1917.
106. Wallace, W. M., and Hastings, A. B. Distribution of bicarbonate ion in mammalian muscle. *J. Biol. Chem.* **144**:637-649, 1942.
107. Rosenbaum, J. D. Influence of alterations in acid-base balance upon transfer of carbon dioxide and bicarbonate in man. *J. Clin. Investigation* **21**:735-746, 1942.
108. Schechter, A. J., Cary, M. K., Carpentieri, A. L., and Darrow, D. C. Changes in composition of fluids injected into peritoneal cavity. *Am. J. Dis. Child.* **46**:1015-1026, 1933.
109. Guest, G. M., and Rapoport, S. Role of acid-soluble phosphorus compounds in red blood cells in experimental rickets, renal insufficiency, pyloric obstruction, gastroenteritis, ammonium chloride acidosis and diabetic acidosis. *Am. J. Dis. Child.* **58**: 1072-1089, 1939.
110. Brinkman, R., Margaria, R., Meldrum, N. U., and Roughton, F. J. W. CO_2 catalyst present in blood. *J. Physiol.* **75**:3P, 1932.
111. Meldrum, N. U., and Roughton, F. J. W. Some properties of carbonic anhydrase, the CO_2 enzyme present in blood. *J. Physiol.* **75**:15P, 1932.
112. Booth, V. H. Carbonic anhydrase inhibitor in serum. *J. Physiol.* **91**:474-489, 1938.
113. Stevenson, S. S. Carbonic anhydrase in newborn infants. *J. Clin. Investigation* **22**:403-409, 1943.
114. Marriott, M. W., Hartmann, A. F., and Senn, M. J. E. Observations on nature and treatment of diarrhea and associated systemic disturbances. *J. Pediat.* **3**:181-191, 1933.
115. Young, E. G., and Smith, R. P. Lactic acid: corrosive prison. *J. A. M. A.* **125**:1179-1181, 1944.
116. Oxyhemoglobin. In *Notes on Operation of Evelyn Photoelectric Colorimeter*. 40 pp. Philadelphia: Rubicon Company. P. 34.
117. Lowry, O. H., and Hastings, A. B. Histochemical changes associated with aging. II. Methods and calculations. *J. Biol. Chem.* **143**: 257-269, 1942.
118. Folin, O. *Laboratory Manual of Biological Chemistry*. Fifth edition. 368 pp. New York: D. Appleton-Century Company, 1934. P. 271.
119. Peters, J. P., and Van Slyke, D. D. Chloride in blood or serum. In *Quantitative Clinical Chemistry*. Vol. 2. Methods. 981 pp. Baltimore: Williams & Wilkins Company, 1932. P. 835.
120. Butler, A. M., and Tuthill, E. Application of uranyl zinc acetate method for determination of sodium in biological material. *J. Biol. Chem.* **93**:171-180, 1931.
121. Van Slyke, D. D., and Neill, J. M. Determination of gases in blood and other solutions by vacuum extraction and manometric measurement. *J. Biol. Chem.* **61**:523-573, 1924.
122. Hastings, A. B., and Sendroy, J., Jr. Studies of acidosis. XX. Colorimetric determination of blood pH at body temperature without buffer standards. *J. Biol. Chem.* **61**:695-710, 1924.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**
BENJAMIN CASTLEMAN, M.D., *Acting Editor*
EDITH E. PARRIS, *Assistant Editor*

CASE 30441

PRESENTATION OF CASE

A seventy-nine-year-old man entered the hospital for study.

For many years before admission the patient complained of urinary symptoms, including frequency and nocturia (six to eight times). There was diminution in the caliber and strength of the urinary stream, with dribbling and intermittency of urination. Six years prior to entry he was told that he had "prostatic trouble." During the few months before admission his urinary difficulties increased in severity.

*On leave of absence.

The past history revealed that the patient had a moderate tremor of the extremities for thirty years and of the head and voice for two years.

Physical examination revealed a well-developed and well-nourished man in no obvious distress. There was bilateral arcus senilis. There was a gross tremor of the head. The chest was moderately emphysematous. The lungs were clear to auscultation and percussion. The heart was slightly enlarged to the left on percussion. The rhythm was normal. There were no murmurs or thrills. Multiple extrasystoles were heard over the apex. The abdomen was negative, except that the bladder was distended, reaching to 5 cm. below the umbilicus. The prostate was twice the normal size, nontender, resilient and movable. There were marked tremors of the extremities and of the voice. Neurologic examination was negative.

The blood pressure was 240 systolic, 104 diastolic. The temperature was 98.6°F., the pulse 80, and the respirations 20.

Examination of the blood showed a red-cell count of 4,750,000, with a hemoglobin of 85 per cent. The white-cell count was 9400. The urine showed a + to +++ test for albumin; the sediment contained innumerable red cells, and a culture revealed abundant *Staphylococcus albus*. The nonprotein nitrogen was 35 mg. per 100 cc.

An x-ray film of the chest showed a slight amount of mottled, increased density in the left upper lobe behind the first interspace. The bases of both lungs were emphysematous. There was a rounded area of calcification 1 cm. in diameter at the right base, which was thought to represent a Ghon lesion. The diaphragm was low in position. There was slight prominence of the left ventricle, but the cardiothoracic ratio was 14:30. An intravenous pyelogram was negative.

On the third day the patient suddenly complained of severe, nonradiating subxiphoid pain accompanied by slight nausea and, two hours later, vomiting. Physical examination revealed an occasional extrasystole in a slightly enlarged heart, with otherwise regular rhythm. There were a split mitral second sound and a faint apical systolic murmur. The lungs were clear. There was no evidence of cardiac failure, and the patient was not cyanotic. The epigastrium was not tender. The legs were normal. The blood pressure was 260 systolic, 120 diastolic. The patient was confined to bed and given 11 mg. (1/6 gr.) of morphine. The pain lasted two hours and then subsided.

Two days later an electrocardiogram revealed normal rhythm, with a rate of 60, a PR interval of 0.17 second, a slightly sagging ST segment, an upright T_1, a low upright T_2 and a small Q_3 (2 mm.) and Q_3 (3 mm.), with deep late inversion of T_3; the precordial leads showed upright T waves, with slightly sagging ST segments in CF_4 and CF_5. The blood pressure was 150 systolic, 60 diastolic. The corrected sedimentation rate was 1.8 mm. per minute.

An electrocardiogram taken on the seventh day after admission revealed a normal rhythm, with a rate of 60, a PR interval of 0.17 second, sagging ST_1, ST_2 and ST_3, an upright T_1, diphasic T_2 and T_3 and small Q_2 and Q_3; the precordial lead showed an upright T wave. An electrocardiogram taken fourteen days after admission showed normal rhythm, with a rate of 80, a PR interval of 0.16 second, an upright T_1, a flat T_2, an inverted T_3, small Q_2 and Q_3, slight slurring of QRS_2 and an upright T in the precordial leads.

In the meantime, beginning with the fifth hospital day, the patient began to run a low-grade fever. The lungs were clear. There was slight tenderness in the costovertebral angle. Urinalysis revealed a sediment containing innumerable white cells. A urine culture showed abundant colon bacilli and nonhemolytic streptococci. A blood culture was negative. On the fourteenth hospital day the patient was put on a course of 0.5 gm. of sulfathiazole every eight hours. He continued to run a temperature of 102°F., but the lungs remained clear, except for a few fine rales at the right base posteriorly. The legs were normal.

A chest plate taken on the twentieth hospital day revealed a large amount of fluid in the posterior costophrenic angle on the right. On the following day bilateral superficial femoral-vein ligations were done. No clots were found. On the twenty-first hospital day the nonprotein nitrogen was recorded as 38 mg. per 100 cc. The white-cell count was 26,600. The patient complained of pain above the symphysis pubis. The pulse rate was 116, with an occasional dropped beat. The chest showed a few rales, slight dullness and decreased fremitus in the left base posteriorly. The abdomen was somewhat distended. He became weaker, drowsier, went into Cheyne-Stokes respiration and had frequent episodes of vomiting.

On the twenty-sixth hospital day the nonprotein nitrogen was 86 mg. per 100 cc. in spite of an excellent fluid intake and a good urinary output. The electrocardiogram showed a rate of 140, a PR interval of 0.14 second, a sagging ST_1, an upright T_1, a sagging ST_2, an upright T_2, a low upright T_3, a wide slurring of QRS_2, small Q_2 and Q_3, an upright T in CF_2, CF_4 and CF_5, and a sagging ST in CF_5. A chest plate revealed less fluid in the pleural cavity. There was moderate pitting edema of both feet, in spite of digitalis and restriction of salt. The patient continued to have abdominal distention and episodes of vomiting.

On the thirty-fourth hospital day he exhibited pitting edema of the hands, arms, legs and sacrum. The total protein was 4.3 gm., and the nonprotein nitrogen 52 mg. per 100 cc. Five days later he suddenly complained of severe precordial constriction, without radiation. Physical examination revealed a tachycardia and a scratchy systolic murmur, loudest at the left border of the sternum. The lungs were clear anteriorly and laterally. The patient was not dyspneic or cyanotic. The neck veins were not distended, nor were they pulsating. An electrocardiogram showed a sinus tachycardia of 150, a PR interval of 0.13 second, sagging ST_1 and ST_2, a low T_1, an upright T_2 and T_3, and a sagging ST in CF_4 and CF_5, with low upright T waves. Six hours after the onset of this attack, on the fortieth hospital day, the patient expired.

Differential Diagnosis

Dr. Paul D. White: This patient was so old that anything could have been wrong with him. He was not acutely ill at first. He came to the hospital for a urologic check-up.

"The heart was slightly enlarged to the left on percussion," a difficult method of examination in the presence of pulmonary emphysema. X-ray study was certainly in order to determine the true size of the heart.

"The prostate was twice the normal size, nontender, resilient and movable." I do not know whether that rules out malignancy, but I believe that it is evidence against it.

There was some hypertension, largely of the arteriosclerotic type, with relatively low diastolic

pressure, as diastolic hypertensions go. The patient had an extremely high systolic pressure for a time; later it came down. There was a pulse pressure of over 100 mm.

There was hematuria, but not much evidence of severe renal infection at that time. Was more than one culture made? There is a strong suspicion of infection, which may have been renal.

What was the specific gravity of the urine?

DR. BENJAMIN CASTLEMAN: The specific gravity was 1.022; following this it was 1.030, and then 1.012, 1.010 and 1.008.

DR. WHITE: There was evidently good concentration, which is of considerable importance.

DR. CASTLEMAN: Only on admission. After the first week it was in the neighborhood of 1.012 and 1.010.

DR. WHITE: "On the third day the patient suddenly complained of severe, nonradiating, subxiphoid pain accompanied by slight nausea and, two hours later, vomiting." Except for the hypertension, this is where the cardiovascular part of the case comes in.

The split mitral second sound was probably not significant, unless interpreted as a gallop rhythm, which was not at all definite and rather unlikely. If we are looking for trouble below the diaphragm, from the standpoint of an abdominal emergency, nausea and vomiting fit in of course; they are not so frequent with cardiovascular accidents but can occur. Also, one must think of the possibility of pulmonary embolism from phlebitis. The legs were, however, said to be normal. The pulse presumably was definitely felt in the feet.

The blood pressure went up under the stimulus of this pain. That sometimes happens, no matter what the fundamental cause may be; it drops only with great prostration and collapse.

We should not make too much of the electrocardiogram, and yet it may give important clues to explain an acute process. The findings here could have been due to a fresh posterior myocardial infarct, three days old. If a record had been taken on the first or second day, perhaps there would have been more evidence of change in the ST segment if a fresh myocardial infarct had occurred. The tracing is not characteristic of acute cor pulmonale in that there is no S wave in Lead 1.

DR. CASTLEMAN: The electrocardiogram was taken forty-eight hours after admission.

DR. WHITE: It was taken reasonably soon after the attack, but the changes would have been more definite in the first twelve hours, especially in the precordial leads. The precordial T wave is high if anything, which helps to rule out an acute cor pulmonale and favors a posterior myocardial infarct. The sagging of the ST segments in Leads CF_4 and CF_5 is also in keeping with that, although it did not last long. The small Q waves are unimpressive.

There was a drop in blood pressure forty-eight hours after the attack.

Another electrocardiogram showed a more pronounced inversion of the T waves in Lead 2 and Lead 3. T_3 is not so deep as before, but there is a greater change in Lead 2, the precordial T waves still being upright, although not so strikingly high. The very height of these T waves makes one think of the possibility of posterior myocardial infarction, for an extremely high T wave is often as significant as an inverted T wave.

There was not a great deal of change in the third electrocardiogram according to the description, mostly a straightening out of the waves; T_3 was flat, and T_2 inverted, although not so deep, again with high T waves in the precordial leads.

How high was the temperature two days after the attack and how high did it go?

DR. CASTLEMAN: It went to 103°F. at one time.

DR. WHITE: That is a fair degree of fever for myocardial infarction alone; in fact, it is higher than one would expect. The lungs were clear, and there was slight tenderness in the costovertebral angle. Urinalysis revealed a sediment containing innumerable white cells. Apparently there was a pyuria. The urine culture showed abundant colon bacilli and streptococci. Much of the fever may have been due to infection in the genitourinary tract.

The patient was put on sulfathiazole, evidently to combat this urinary infection. Probably his physicians thought that the fever was due to infection rather than to the process that was responsible for the substernal pain.

"The legs were normal." They were still looking hard for a source of embolism.

In addition to the information about the chest I should like to know how large the heart was and about the aorta, because in some of these accidents we have to think of dissecting aortic aneurysm, which may involve the renal circulation.

DR. LAURENCE L. ROBBINS: These are the films referred to first. There is a small amount of fluid in the posterior costophrenic angle. The shadow that appears to be within the lungs possibly represents a small area of infarction. In subsequent films, there is rather marked change in the appearance of the vascular shadows in the lung fields. They have increased in size. I cannot be sure of the heart measurements because the film was taken to demonstrate the lung fields rather than the heart. This film gives a fairly accurate idea of the size of the heart. There is no enlargement, but there is evidence of left ventricular hypertrophy.

DR. WHITE: Was that taken before the attack?

DR. ROBBINS: Yes.

DR. WHITE: Despite the systolic hypertension, the heart was not particularly large for a patient of seventy-nine; evidently he supported the systolic

hypertension extremely well, but we do not know how long he had had it.

DR. ROBBINS: There does not appear to be much increase in the size of the heart. In this film, taken later, there is evidence of an increase in pulmonary congestion, and the shadow seen in the previous film is obscured by a high diaphragm.

DR. WHITE: It looks as if there were less fluid.

DR. ROBBINS: I am not certain about the amount of fluid because the film was taken with the patient on his back, and the diaphragm is higher than in the previous films. There might be some fluid.

DR. WHITE: The report says there was "less pleural fluid."

DR. ROBBINS: That is true, but if the fluid gravitated posteriorly in the chest one would see a sharp costophrenic angle and not much fluid.

DR. WHITE: There must have been strong clinical evidence of pulmonary embolism or infarction, since the leg veins were ligated.

The leukocytosis was too high for an infarct of the heart or lung without complications. I think that this indicates that more than one thing was wrong; the genitourinary complication doubtless enters in here.

Is there indication of fluid in the left base?

DR. ROBBINS: No.

DR. WHITE: The patient then became uremic.

The PR interval decreased, characteristic of an increased heart rate, and T_3 came back to a more normal appearance. There is no apparent evidence of a fresh myocardial infarction.

"The total protein was 4.3 gm." That, as well as the renal state, may account for part of the edema.

"He suddenly complained of severe precordial constriction without radiation." Apparently this was not the same as the pain that occurred several weeks previously. It was again precordial, however, although not necessarily substernal; there was constriction. I wonder if he was dyspneic at that time; there is no statement to that effect.

I also wonder whether the pericardial friction rub might have been the result of uremia or of a distended right ventricle and pulmonary artery following pulmonary embolism. There was no evidence of heart failure at that time to explain the fluid in the chest.

In summary, the patient certainly had prostatic hypertrophy and obstruction, quite mild, with retrograde infection of the urinary tract, including pyelitis and terminal uremia. I shall hazard a guess that he had pericarditis resulting from uremia. There was also hypertension, of the systolic type, not causing much cardiac enlargement originally; there was slight left ventricular enlargement, with increase in size of the heart, after the first acute episode, which I shall interpret as posterior myocardial infarction. I shall add to that a diagnosis of terminal pulmonary embolism and infarction — in these older patients, the more diagnoses the better. Also there was anasarca due to a combination of several factors — renal disease, hypoproteinemia and, perhaps, heart failure.

DR. CONGER WILLIAMS: This patient was on our service last month. I thought that the first episode probably represented myocardial infarction. His veins were tied because there was a suspicion of pulmonary infarction and we thought that it could do no harm. Later many things developed, including terminal uremia. When the final episode started was of no more than academic interest because of other things that had occurred; I thought that the last episode was suggestive of pulmonary embolism, even though the veins had been tied off. Such a thing does happen.

DR. WHITE: The first attack was different from the second?

DR. WILLIAMS: I did not see the patient in the last attack, but as it was described to me it sounded as if it were due to pulmonary embolism.

DR. HOWARD B. SPRAGUE: Do you think that he had a pulmonary embolus that arose in the right heart following the basal infarct?

DR. WHITE: Such a condition is rare.

DR. SPRAGUE: I know it, but I recently had a case.

DR. WHITE: It is possible, but I should not make that diagnosis.

CLINICAL DIAGNOSES

Benign prostatic hypertrophy.
Chronic pyelonephritis.
Uremia.
Old pulmonary infarct with bilateral vein ligations.
Recent myocardial infarction?

DR. WHITE'S DIAGNOSES

Prostatic hypertrophy and obstruction.
Pyelitis.
Uremia.
Pericarditis, uremic.
Hypertension, with slight cardiac hypertrophy.
Posterior myocardial infarction.
Hypoproteinemia.
Anasarca.
Pulmonary embolism and infarction, terminal.

ANATOMICAL DIAGNOSES

Myocardial infarction: left ventricle and posterior part of septum.
Interstitial myocarditis and generalized perivascular cellular infiltration (sulfonamide idiosyncrasy).
Cardiac hypertrophy, hypertensive type.
Pyelonephritis, acute and chronic.
Prostatic abscesses.

Adenocarcinoma of prostate.
Cystitis.
Hydrothorax, bilateral.
(Uremia.)

Pathological Discussion

Dr. Castleman: The autopsy showed an enlarged heart, weighing 420 gm., of the hypertensive type, the hypertrophy being left ventricular. In the right coronary artery, 9 cm. from its origin, we found an occluding recent organizing thrombus, the age of which would fit in with the time of the attack that he had had on the third hospital day. The circumflex and descending branches of the left coronary artery were markedly sclerotic, but there was no evidence of occlusion.

The myocardial infarction was limited to the posterior wall of the left ventricle, although there were some tiny grayish-red areas in other parts of the heart that we could not explain. There were no infarcts in the lung, and no evidence of pulmonary emboli.

There was 500 cc. of fluid in each chest cavity, but none in the abdomen.

Both kidneys were markedly enlarged and swollen, and we thought that grossly they suggested a pyelonephritis. The bladder showed a mild cystitis. The prostate was enlarged to twice the normal size, showing considerable necrosis and infection. In one area there was a small but definite adenocarcinoma. There was no evidence of extension of the neoplasm around nerves, and no evidence of metastasis anywhere in the body.

Microscopic sections of the heart showed, first, the obvious infarct of almost a month's duration. Sections away from the infarct and corresponding to the location of the pinpoint grayish-red areas observed grossly showed an interstitial myocarditis. There was a cellular infiltration, consisting mostly of eosinophils and monocytes, in the interstitial tissues, especially around the blood vessels (Fig. 1). These findings are quite similar to those of interstitial myocarditis due to sulfonamides, first observed by French and Weller.[1] Similar perivascular infiltrations were found in the lungs (Fig. 2) and in one section of smooth muscle. I believe that these changes followed the sulfonamide therapy, apparently a hypersensitivity reaction. Perhaps this is the early stage of the frank periarteritis that has been described by Rich.[2] There were similar areas in the kidney, but one cannot be sure that they were due to sulfonamides. The patient had a severe pyelonephritis, and they can be explained on that basis. In a case of severe sulfonamide nephrosis, which we discussed here a year ago,[3] the myocardium showed exactly the same picture — eosinophilic, lymphocytic and monocytic infiltration in the interstitial tissues and around the vessels.

It is quite possible that some of the changes in the electrocardiogram may have been due to these lesions. Dr. Bernard Maisel, who worked in our laboratory a year or so ago on sulfonamide intoxications, has just told us about a patient who

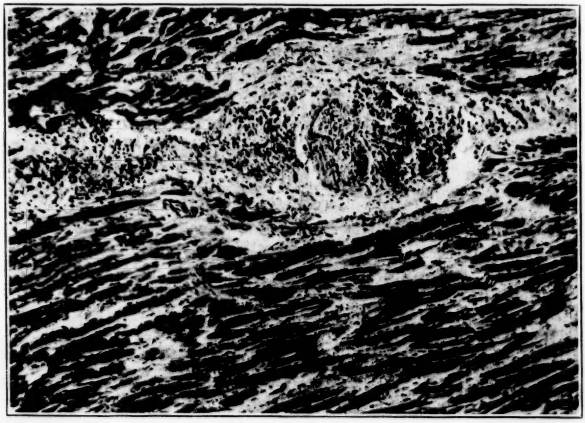

Figure 1. *Photomicrograph of Section of Heart Muscle.*

received sulfonamides prophylactically before an intestinal resection for carcinoma and who after the operation developed signs of cardiac failure with queer electrocardiographic changes; at autopsy the myocardium showed severe interstitial myocarditis.

DR. WHITE: In this case, some of the later changes did not fit in with the myocardial infarct, although there was clear evidence thereof in the first few. It is conceivable that the sulfonamide myocardial changes might have altered the electrocardiogram, but we need more information to be certain.

Was the heart dilated?

DR. CASTLEMAN: Yes.

DR. WHITE: Hence, congestive heart failure might have accounted for some of the fluid in the chest.

REFERENCES

1. French, A. J., and Weller, C. V. Interstitial myocarditis following clinical and experimental use of sulfonamide drugs. *Am. J. Path.* **18**:109-121, 1942.
2. Rich, A. R., and Gregory, J. E. Experimental demonstration that periarteritis nodosa is manifestation of hypersensitivity. *Bull. Johns Hopkins Hosp.* **72**:65-88, 1943.
3. Case records of the Massachusetts General Hospital (Case 29211). *New Eng. J. Med.* **228**:687-690, 1943.

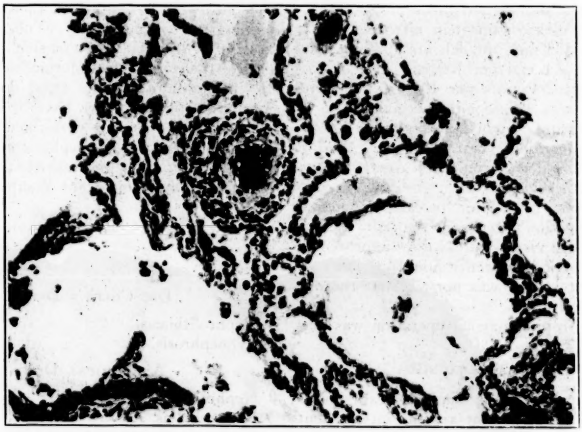

FIGURE 2. *Photomicrograph of Section of Lung.*

CASE 30442

PRESENTATION OF CASE

A forty-three-year-old railroad worker was admitted to the hospital with pain in the region of the left costovertebral angle.

The patient was apparently in good health until two years prior to admission, at which time he had an attack of severe stabbing pain in the region of the left costovertebral angle, radiating to the left groin. Similar attacks, each lasting a few seconds, recurred at intervals of once or twice a week. He developed urinary frequency of about six to seven times daily and twice nightly. He also had pain and discomfort in the right upper quadrant, as well as abdominal distention at times. There was no jaundice, nausea or vomiting. One month prior to admission the attacks increased in frequency and severity, occurring daily. At no time did he notice hematuria or pyuria, nor did he pass any gravel. He had lost 14 pounds over a period of six months. Because of his symptoms he visited the out-patient department of another hospital, where urograms were taken. These showed a huge left hydronephrosis with multiple calculi in the pelvis and calyxes and no function. The right kidney was poorly visualized but was apparently normal in outline and pattern.

Except for the fact that the patient had been consuming four to five quarts of alcohol weekly over a period of five to six years, the past and family histories were noncontributory.

Physical examination revealed a well-developed man who appeared chronically ill. The heart and

lungs were normal. The left kidney was readily palpable, and left costovertebral angle tenderness was present. The spleen could not be felt.

The blood pressure was 130 systolic, 70 diastolic. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 3,350,000, with 60 per cent hemoglobin, and a white-cell count of 12,500. A voided specimen of urine had a specific gravity of 1.010, with a ++ test for albumin and many red and white cells in the sediment. The blood nonprotein nitrogen was 26 mg., the sugar 123 mg., the calcium 10.7 mg., and the phosphorus 4.4 mg. per 100 cc. The alkaline phosphatase was 2.4 units per 100 cc. The prothrombin time was 14 seconds (normal, 18 to 20 seconds). The serum protein was 6.9 gm. per 100 cc., with an albumin-globulin ratio of 1.4. A urine culture showed a few colonies of *Staphylococcus albus* and diphtheroids.

An intravenous pyelogram revealed numerous areas of calcification overlying the left kidney, which was not well visualized. No dye appeared on the left over a period of twenty minutes. The outline of the right kidney was normal, and the dye appeared promptly.

On the fifth hospital day an operation was performed.

Differential Diagnosis

Dr. Fletcher H. Colby: The significant points in the history of this patient are the intermittent attacks of left costovertebral pain over a two-year period, which radiated to the groin at the outset. There was moderate frequency of urination, but no gross hematuria; and no stones were passed. Prior to admission the frequency increased and there was considerable loss of weight. Urograms were said to have been taken at another hospital that demonstrated a huge left hydronephrosis with multiple calculi; since this kidney undoubtedly had no function at that time, a retrograde pyelogram must have been done to visualize the renal pelvis.

The history suggests, of course, left renal colic, with stones as the likeliest cause. Such symptoms, however, may be due to other conditions, such as renal tumor, usually associated with the passage of blood clot, and various obstructive congenital lesions. Gastrointestinal symptoms are frequently produced by a fairly advanced lesion of the kidney, because of pressure on neighboring organs from a large renal mass or possibly reflexly through the sympathetic nervous system.

On physical examination the left kidney was sufficiently enlarged to be readily felt and there was left costovertebral angle tenderness. Moderate anemia was present. The urine was low in specific gravity and contained both blood and pus. The blood chemical findings, with normal calcium, phosphorus and protein determinations, appear to eliminate parathyroid disease. *Staph. albus* and diphtheroids were found in the cultured urine. The diphtheroids are contaminants, but the staphylococcus is probably significant since some strains of this organism invade the urinary tract and are capable of separating urea, thus favoring stone formation by the strongly alkaline urine that is produced.

At x-ray examination the many areas of calcification are typical of stones scattered throughout a dilated, badly damaged, functionless left kidney. There is no good reason to suspect tumor from the evidence we have, although there is no method of eliminating this possibility. Tuberculosis is seldom associated with such extensive stone formation. One of the congenital abnormalities may have been the background for the renal damage and stone formation, but again we have no definite evidence of this. The operation performed on the fifth day was presumably a left nephrectomy for a calculus pyonephrosis. The appearance of the stones by x-ray suggests that they were composed of calcium phosphate.

Clinical Diagnoses

Nephrolithiasis.
Pyonephrosis.

Dr. Colby's Diagnoses

Nephrolithiasis.
Pyonephrosis.

Anatomical Diagnoses

Nephrolithiasis.
Pyonephrosis.
Carcinoma in situ and epidermoid carcinoma of renal pelvis, multiple.

Pathological Discussion

Dr. Benjamin Castleman: This case was used in these exercises to illustrate one of the extremely rare conditions occurring with renal stones. As Dr. Colby predicted this patient did have a large pyonephrotic fluctuant kidney, with obliteration of most of the parenchyma by the dilated calyxes (Fig. 1). There were several large stones within the pelvis and calyxes. The unusual finding was the presence of several grayish-white, slightly raised, granular areas about 2 cm. in diameter on the mucosal surface of the pelvis and some of the calyxes. In a few places these apparent tumors extended into the parenchyma. In other areas the mucosa was merely roughened.

Microscopic examination revealed all stages in the development of epidermoid carcinoma. The slightly roughened areas showed a marked atypicality and anaplasia of the epithelium but no evidence of invasion — a condition that we call "carcinoma in situ" (Fig. 2). Other areas showed early invasion with extensive keratinization — a Grade I epidermoid carcinoma (Fig. 3). In the grossly invading foci the carcinoma was a bit less differentiated and might be classified Grade II or III.

Although it cannot be proved, the presence of

multiple foci of carcinoma in all stages of development associated with multiple renal stones suggests that the chronic irritation of the calculi led to the formation of the neoplasms.

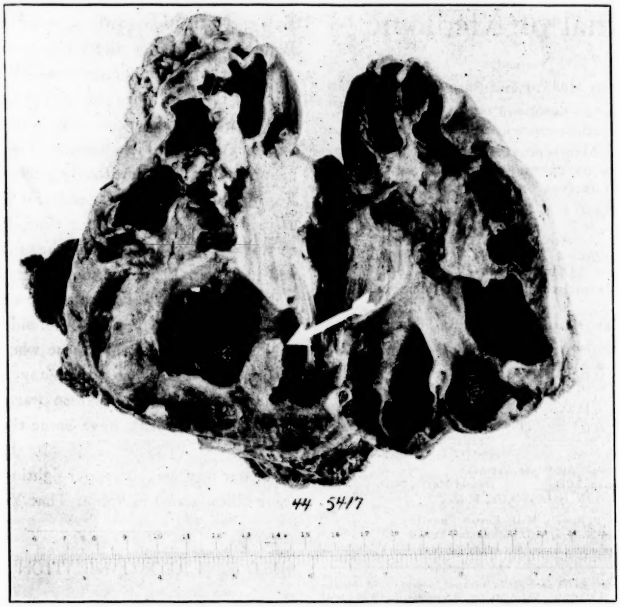

FIGURE 1. *Photograph of the Bisected Kidney.*
The arrow points to one of the granular areas mentioned in the text.

FIGURE 2. *Photomicrograph of a Section of the Kidney. This area shows carcinoma in situ of the pelvic epithelium.*

FIGURE 3. *Photomicrograph of a Section of the Kidney. This area shows epidermoid carcinoma of the renal pelvis.*

DR. COLBY: The curious appearance of the kidney certainly suggests that the stone formation antedated the neoplasm. It therefore seems reasonable that the continued irritation of the stones and the infection had a great deal to do with the formation of the carcinoma. There have been a sufficient number of similar cases reported in the literature to support this point of view.

The New England Journal of Medicine

Formerly

The Boston Medical and Surgical Journal

Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D.

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

Editorial Board

Joseph Garland, M.D. A. Warren Stearns, M.D.
Shields Warren, M.D. Dwight O'Hara, M.D.
C. Guy Lane, M.D. Chester S. Keefer, M.D.
William A. Rogers, M.D. Howard M. Clute, M.D.
Stephen Rushmore, M.D. Fletcher H. Colby, M.D.
Henry R. Viets, M.D. Robert L. Goodale, M.D.
Robert M. Green, M.D. Chester M. Jones, M.D.
Charles C. Lund, M.D. Harvey R. Morrison, M.D.

Associate Editors

Thomas H. Lanman, M.D. Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year (Boston funds); $8.52 per year for all foreign countries belonging to the Postal Union.

Material should be received not later than noon on Thursday, two weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

UNITED WAR FUND

From now until November 23 the Greater Boston United War Fund will be holding its campaign to raise $7,650,000 for home-front and war-related appeals.

On meeting the home-front needs depends the physical and social health of the community. Two hundred and sixty-seven hospitals, clinics, dispensaries and youth and social services are affiliated with the Fund. Physicians need not be told of the work these services do; indeed, physicians give generously of their time and energy to serve the health of the community, and day after day see for themselves the needs of those whom they and these agencies serve.

In a world seething with hate and killing, our own community is only a small part of our responsibility. Every contribution to the Greater Boston United War Fund is also a direct gift to some homesick soldier or weary sailor overseas. We give to our men in uniform when we give to the USO, the United Seamen's Service, the War Prisoners Aid and the American Field Service. The needs of these men will not be immediately decreased when the European phase of the war ends, for the repatriation of prisoners will take a long time, large armies of occupation must be kept, and the problem of morale will increase. Then, too, our efforts in the Pacific will be increased, and these services must be ready for still larger tasks on the other side of the world.

Not less important are those who have suffered far more and far longer than any of us. United Nations Relief goes to sixteen war-ravaged countries, whose occupants have borne the brunt of the fight.

For our own neighbors, our fighting men and our brave allies, give and "Show That You Care."

NEED FOR REORGANIZATION

Although, by and large, during the last two years the people of the United States have not truly suffered from the lack of medical, nursing and hospital care, a number of situations have arisen that have already resulted in the lowering of standards of which this country had just reason to be proud. Furthermore, it seems likely that many, if not all, of these blunders might have been avoided if a broader and more knowledgeable attitude had been taken regarding the demands for medical and nursing personnel by the Army and Navy, particularly the former.

The men in the armed forces deserve the best of medical care, — and this they are undoubtedly receiving, — but unlike butter, the physician and the nurse are commodities that the civilians, the majority of whom are contributing in one way or another to the war effort, cannot do without. To cut down below a certain level, as well as to accelerate medical education, creates conditions that eventually undermine the health of the population. Already there is a shortage of hospital beds that

might be catastrophic in the event of a nation-wide epidemic, and the average number of days of hospitalization has been prolonged, both of which are largely due to a depleted medical and nursing personnel. Medical-school graduates, to say nothing of faculty members, are tired and confused by three years of accelerated teaching, and hospitals obviously cannot give adequate practical training during a nine-month rotating internship or under the 9–9–9 plan. Finally, deferment has been denied to premedical students at a time when the number enrolled under the Army and Navy training programs has been drastically cut; this can only result in a diminution in the number of properly qualified students.

The educational aspect is forcefully brought to the attention of the medical profession by Dr. Evarts A. Graham in an editorial published in the August issue of *Surgery, Gynecology and Obstetrics*, which reads as follows:

> The medical schools and civilian teaching hospitals of this country are engaged in the education of medical officers for the armed services. . . . That the efforts of the medical schools and teaching hospitals have been successful is attested by the extravagant praise accorded, especially, to the surgeons in the Army and Navy for the astonishingly high percentage of wounded men returned to active duty. . . .
>
> The surgeons who are responsible for this splendid record are men who not only had the benefit of four years in a medical school following a good premedical training in the colleges but in addition spent several years in special training in our civilian teaching hospitals. Many also have fulfilled the requirements for fellowship in the American College of Surgeons and for certification by the American Board of Surgery. . . . The Army has recognized the importance of [such] qualification . . . by giving a certain amount of preferential consideration to the members of the College and particularly to those who hold certificates of the American Board.
>
> This splendid plan, however, . . . has been scrapped by the War and Navy Departments. Laymen . . . have dictated what may be given in a premedical course, have streamlined the medical course itself and have practically destroyed the resident system of training. Many medical officers will now enter the army to serve in battalion aid stations and in other places demanding a knowledge of surgery whose maximum graduate hospital experience has been nine months of a rotating intern service with perhaps only two months in surgery. Is this the kind of medical officer the armed forces want? Pity the wounded if it is!
>
> Let us imagine a group of surgeons with the authority to prescribe the education of line officers, be they Army or Navy. Would they wreck West Point and Annapolis? Would they reduce their faculties by 40 or 50 per cent at the same time that they increase the number of the students? Would they reduce the period of training of artillery officers or submarine commanders to an amount which could not possibly make them efficient? It seems unlikely that they would. . . .
>
> Is the medical officer of less value than the line officer? The General Staff may think so, but we know full well that a modern army could not function at all without its medical department. . . .
>
> Although the Surgeon General . . . is no longer a member of the General Staff, the Army must appreciate the value of the medical officers because it wants so many of them even if they are only half-baked. In fact much of the present difficulty arises because of the large number wanted. At the outbreak of the present war we were told that the army needed 6.5 medical officers for each 1000 men in the Army. . . .
>
> The demand for so large a number of medical officers is the fundamental cause of the disruption of the prewar efficient plan for their education. . . . Shall we send our men into battle with Civil War muskets if the supply of modern arms is deficient? Of course not. Anybody can see how ridiculous and murderous that would be. But perhaps only doctors themselves can appreciate how murderous a half-baked medical officer can be.
>
> Is it necessary that this large number of medical officers be provided? If it is then everybody will be glad to make the best of it. The armies of other countries have not been furnished with anything like so high a proportion of medical officers. The British, the Australian, and the Canadian armies, for example, get along with a proportion only a little more than half of what is felt necessary by our armed forces; and the quality of the work done is excellent. . . . Is not this demand for so many medical officers an unjustifiable extravagance for which there is no demonstrated need?
>
> These remarks have been directed at the evil effects upon the medical officers themselves caused by the disruption of the only plan for developing properly trained surgeons which has ever been found to work. A similar editorial could be written on the disaster to the civilian population. Are we to go backward a quarter of a century and to surrender to our two great allies the enviable position in medicine which this country occupied before the war? The British Commonwealth and Russia have not found it necessary to disrupt their medical education to anything like the extent which we have been forced to do. As a result we may find ourselves a poor third in medicine in the postwar world. Is it necessary? I know of no convincing evidence that it is. But nothing will be done to remedy the situation unless the medical profession itself, the only body capable of understanding how a medical officer should be educated, speaks its mind loud enough for Congress and the President to hear. Reduce the 6.5 ratio to a reasonable one and much of the basis for the wrecking of our medical education will disappear. The 9–9–9 plan will not train surgeons and will not provide competent surgical officers. Still less will the nine months' rotating internship. That plan should be scrapped and in its place a reasonable program for the training of medical officers should be substituted immediately after a proper inventory of the real needs of the armed services has been made. . . .

Dr. Graham's plea for "a reasonable program for the education of medical officers . . . after a proper inventory of the real needs of the armed

forces" seems justified, and it is likely that this would result in the correction of the other faults. As he suggests, and as Dr. Loyal Davis claims in an editorial published in the September issue of *Surgery, Gynecology and Obstetrics*, the chief source of trouble, at least so far as the Army is concerned, stems from the fact that the Medical Department, a relatively independent unit prior to February, 1918, is part of the Army Service Forces; the Surgeon General and the medical officers in combat zones are under the control of the General Staff, which includes no medical officer, with the result that all matters of policy must be approved or presented for higher consideration by line officers. Due credit should be given to the Directing Board of the Procurement and Assignment Service for being able to maintain the minimum required medical personnel on the home front, thus giving to the Army every physician who could be spared; on the other hand, this board's power is limited, and proper co-operation can be hoped for only if the Medical Department is completely reorganized. The Surgeon General of the Navy is not handicapped by such limitations, and as Dr. Davis points out, the Surgeon General of the Russian Army is directly responsible only to the Chief of Staff. A similar arrangement should obtain in the Army of the United States, and the medical profession should so inform their representatives in Washington, with the hope that the latter will act with courage and force.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

HALTON — Edward P. Halton, M.D., of Holyoke, died October 18. He was in his sixty-third year.

Dr. Halton received his degree from Yale University School of Medicine, New Haven, in 1905. He was a member of the American Medical Association.

His widow, two sons and a sister survive.

NOTICES

AMERICAN FEDERATION FOR CLINICAL RESEARCH

An all-day meeting of the Eastern Section of the American Federation for Clinical Research is being planned for December 9. Investigators desiring to read papers on clinical research should submit an abstract of not over 200 words to Dr. Orville Bailey, Harvard Medical School, 25 Shattuck Street, Boston 15, before November 15. The meeting will be held in Boston and will be open to members of the medical profession.

BOSTON SOCIETY OF BIOLOGISTS

A meeting of the Boston Society of Biologists will be held in the Main Lecture Room of the Harvard Biological Laboratories on Wednesday, November 15, at 8 p.m.

PROGRAM

Milkman's Disease. Dr. F. Albright.
On the Enzymatic Splitting of Lecithin in Animal Organs. Drs. G. Schmidt and S. J. Thannhauser.
Werner's Syndrome (Progeria of the Adult) and Rothmund's Syndrome. Dr. S. J. Thannhauser.

FORUM ON ALLERGY

The seventh annual Forum on Allergy will be held in the Hotel William Penn, Pittsburgh, Pennsylvania, on Saturday and Sunday, January 20 and 21, 1945. This is a meeting to which all physicians are most welcome, and where they are offered an opportunity to bring themselves up to date in this rapidly advancing branch of medicine by two days of intensive postgraduate instruction. For instance, the twelve study groups, any two of which are open to him, are so divided that those dealing with ophthalmology and otolaryngology, pediatrics, internal medicine, dermatology and allergy run consecutively. In addition, the study groups are arranged on the basis of previous registration. In this way, as soon as the registrations are completed, the registrant is expected to write the group leader and tell him just what questions he wants brought up in the discussion. Attention is also called to the fact that during these two days almost every type of instructional method is employed — special lectures by outstanding authorities, study groups, pictures, demonstrations, symposiums and panel discussions. Further information may be obtained from Jonathan Forman, M.D., 956 Bryden Road, Columbus 5, Ohio.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 9

FRIDAY, NOVEMBER 10
9:00-10:00 a.m. Review of Electroencephalograms Made on Pratt Diagnostic Hospital Cases. Dr. John A. Abbott. Joseph H. Pratt Diagnostic Hospital.
10:50 a.m. Postgraduate clinic in dermatology and syphilis. Dowling Amphitheatre, Boston City Hospital

MONDAY, NOVEMBER 13
12:00 m.-1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, NOVEMBER 14
9:00-10:00 a.m. Newer Diuretics. Dr. Werner Lipschitz. Joseph H. Pratt Diagnostic Hospital.
*12:15-1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, NOVEMBER 15
New England Oto-Laryngological Society. Massachusetts Eye and Ear Infirmary.
9:00-10:00 a.m. Present-Day Treatment of Hypertension. Dr. David Ayman. Joseph H. Pratt Diagnostic Hospital.
*12:00 m. Clinicopathological conference. Children's Hospital.
8:00 p.m. Boston Society of Biologists. Harvard Biological Laboratories.

*Open to the medical profession.

NOVEMBER 8 and 9. National Committee for Mental Hygiene. Page 570, issue of October 19.

NOVEMBER 9. The Clinical and Roentgenological Diagnosis of Carcinoma of the Lung. Dr. Merrill Sosman. Pentucket Association of Physicians. 8:30 p.m., Haverhill.

DECEMBER 9. American Federation for Clinical Research. Notice elsewhere on this page.

DECEMBER 13, and JANUARY 3 to APRIL 25. Metropolitan State Hospital. Page 508, issue of October 5.

JANUARY 20 and 21. Forum on Allergy. Notice elsewhere on this page.

FEBRUARY 19. American Board of Internal Medicine. Page 436, issue of September 21.

(*Notices continued on page xvii*)